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THERAPEUTIC MASTOIDOCENTESIS IN PSEUDOMONAS-MASTOIDITIS

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Pseudomonas pyocyanea is a malevolent bacteria. Secondary infection of acute otitis with this agent can cause mastoiditis. It is shown that local instillation of colistin is efficacious in the treatment of such cases, and seems to be specially valuable because of the risk of further spread of this inflammation during operation without proper control of the pseudomonas infection. Two cases of acute mastoiditis caused by *Ps. pyocyanea* were successfully treated with mastoidocentesis, i.e. puncture of the mastoid process and with repeated local deposition of highly concentrated colistin solution. The patients made a rapid recovery and no side effects were noticed during treatment at follow-ups 6 and 12 months later. Mastoidocentesis and deposition of appropriate antibiotics may also be used in other middle ear diseases, and in selected cases it may provide a useful alternative to mastoidectomy.

Pseudomonas pyocyanea (*Pseudomonas aeruginosa*) is a gram-negative bacillus of low pathogenicity but long known to cause a number of serious complicating infections of the urinary tract, of the eye, ear and of burns, for example. This micro-organism is rarely found in normal auditory canals, but it can be cultured in 70–75% of all cases of external otitis. The bacillus is then believed to be a secondary invader (Perry, 195 ; Senturia, 19 7). *Pseudomonas pyocyanea* is rarely the primary causal agent of acute otitis media (Rudberg, 1954; Grönroos *et al.*, 1964), but it is often demonstrable in discharge obtained a few days after onset, especially in children (Papp & Kaszás, 1960). According to Glanzmann (1950) and Paul & Marget (1963), pseudomonasotitis is not uncommon in infants but then often secondary to other infectious foci.

All inflammations caused by *Ps. pyocyanea* are attended by the obstinate production of typical green pus, and in acute otitis media the pseudomonas infection may progress to uncomplicated or complicated mastoiditis. Paul & Marget suggest that mastoidectomy alone can increase the risk of intracranial complications and therefore recommend specific antibiotic therapy preoperatively in such cases.

In vitro *Ps. pyocyanea* is susceptible to several antibiotics (e.g. streptomycin, polymyxin B, neomycin and kanamycin) which, with but one exception, carry risks of serious side effects. The exception is colistin. This

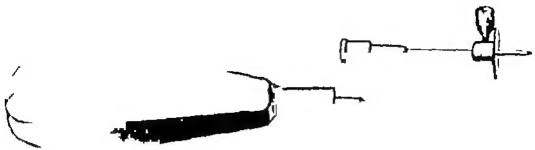

FIG 1 Puncture needle

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Puncture of the Air Cell System in the Mastoid Process

For controlling an infectious focus in the mastoid process the antibiotic must reach the focus and in adequate concentration Therefore local deposition of an antibiotic would give a much higher concentration of the preparations in the focus than what could be obtained by systemic administration But the antibiotic should not be directly resorbable from the middle ear to inner ear with ototoxic damage as a result Administration of an antibiotic via the external auditory canal will not reach a mastoid focus in therapeutic concentration this can solely be obtained by direct deposition in the mastoid process

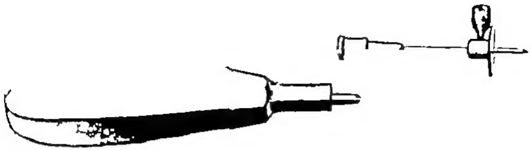
The mastoid puncture technique was first reported by Lallement and coworkers in 1930 and later by Levesque (1943) who treated cases of acute otitis media and of latent mastoiditis by irrigation of the middle-ear

Fig. 2. Puncture needle inserted ready for irrigation.

system via a puncture of the antrum from the outside and deposition of sulphonamide.

Link (1948, 1950) reported that he had since 1943 performed about 1500 *diagnostic* and therapeutic punctures with aspiration and irrigation of the mastoid antrum in infants with occult mastoiditis. Link punctured the planum mastoideum with a 1 mm cannula 2–3 millimetres behind the attachment of the concha under the temporal line *at the level* of the roof of the external auditory canal. Aspiration of air, mucus or bloody secretion, or escape of injected physiological saline solution through the external meatus or via the Eustachian tube into the nose showed that the tip of the needle was in the antrum. Irrigation alone or combined with the injection of sulpha or penicillin preparation in the cases of mastoiditis resulted in healing in 78%. Puncture was not followed by any serious complications in spite of the fact that in 2 cases the needle was advanced into the cranial cavity. Link therefore considered this technique as safe.

Mülfay & Török described a similar method for the treatment of mastoiditis in adults (1959). They reported 4 cases of acute mastoiditis in which the tip of the mastoid process was punctured with a special needle. They checked that the needle was situated in the air cell system in the same way as Link and then injected antibiotics, especially chloramphenicol and tetracycline into the middle-ear system. They reported that all cases



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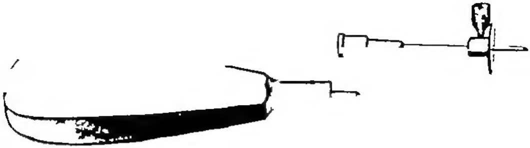

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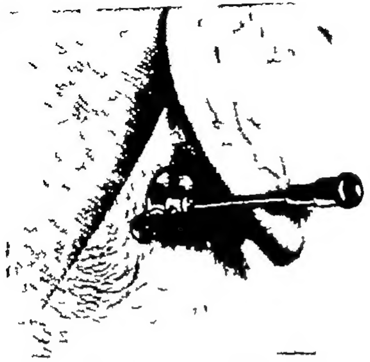

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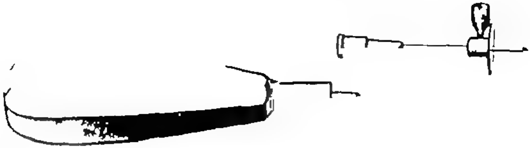

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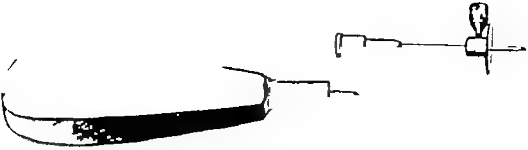

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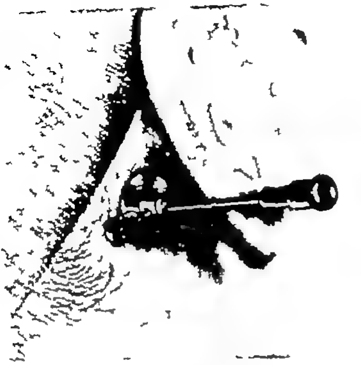

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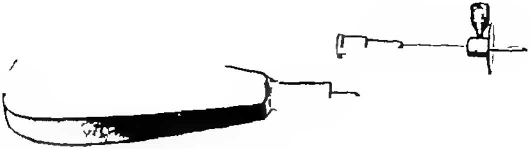

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TABLE 1 *Changes in the optic reflexes induced by optic training (guinea-pig No 2)*

sm = small; l = slight m = medium l = large.

Course of training	Direction of cylinder rotation	Head position, degree of deviation	Head nystagmus, frequency amplitude	Eye nystagmus, frequency amplitude
Prior to training	to right	1st, sl	10, sm	32, sm
	to left	1st, sl	11 sm	34 sm
6th day of training	to right	1st, l	12, sm	46, sm
	to left	1st, l	20, sm	45, sm
12th day of training	to right	1st, m	18, l	44, m
	to left	1st, m	16, l	41 m
20th day of training	to right	1st→3rd, m	16, m	45, l
	to left	1st→3rd, m	18, m	43, l

Results obtained in the other experimental animals

The results obtained in the other guinea pigs, i.e. Nos. 2 and 3 are shown in Tables 1 and 2 The terms 1st, 2nd and 3rd position appearing in the table are defined as follows 1st position is that of the head deviating in the same direction as that of cylinder rotation. 2nd position means the median position of the head. 3rd position is that of the head deviating opposite to cylinder rotation, or deviating so as to counteract the flow of the black lines of the optic cylinder

Thus, 1 t → 3rd position for example means that the head deviated in the same direction as that of cylinder rotation at an early period of optic stimulation, came to deviate in the direction opposite to cylinder rotation on further continuation of the stimulation. As for the degree of the head deviation, "slight" deviation indicates the deviation within 1 cm from the base-line in the record, "medium" deviation indicates the one from 1 cm to 2 cm from the base-line and "large" deviation means the one of more than 2 cm from the base line A for description of the head nystagmus, small medium" and large are used "small" refers to the amplitude less than 1 cm in the record, "medium" to the one from 1 cm to 2 cm, and large" to the one more than 2 cm respectively For the recording of the eye nystagmus, the apparatus was set in such a condition that the amplitude of standard calibration of 200 μv/sec was about 10 mm. Amplitude of the eye nystagmus was described as "small" (less than 3 mm) "medium" (from 3 mm to 6 mm) or "large" (more than 6 mm)

The results obtained in Nos. 2 and 3 showed some differences in detail from the result in No. 1 However it is worth noting that through optic training these cases also showed essentially the same type of modification of the optic reflexes as those observed in No 1

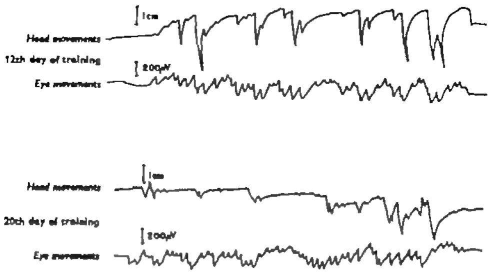

FIG. 2 Recordi gs f the head and the eye movement caused by optic timulation after optic training The upper part of the figure indicates a recording f the head and the eye movement on the 12th day of the training, and th lower part th m v ments on the 20th day of the training In each part f the figure the upper line shows the head movem nts, nd the lower the eye m vements.

Fig 2 right rotation of the optic cylinder caused a distinct right deviation of the head The head nystagmus increased its amplitude markedly but rather reduced its frequency and showed 23 jerks in 40 seconds During the eye nystagmus to the left of increased amplitude we recorded 47 jerks in 40 seconds

Left rotation of the optic cylinder caused a marked left deviation of the head During the head nystagmus to the right, of medium amplitude we noted 10 jerks in 40 seconds During the eye nystagmus to the right of medium amplitude we recorded 53 jerks in 40 seconds

(iv) *On the 20th day of the training* As shown in the lower part of Fig 2 when the optic cylinder was rotated to the right the animal responded to this optic stimulation by turning its head moderately to the left and taking up the head position which seemed to counteract the flow of the black lines of the optic cylinder The head nystagmus to the left became smaller in amplitude and reduced in frequency and showed 21 jerks in 40 seconds However the eye nystagmus to the left was still of large amplitude and showed 50 jerks in 40 seconds

When the optic cylinder was rotated to the left the head deviated slightly to the left However as the optic stimulation was continued further the head of the animal turned to the right and took up the head position which seemed to counteract the flow of the black lines of the optic cylinder During the head nystagmus to the right of less amplitude we noted 4 jerks in 40 seconds During the eye nystagmus to the right of large amplitude we observed 52 jerks in 40 seconds.

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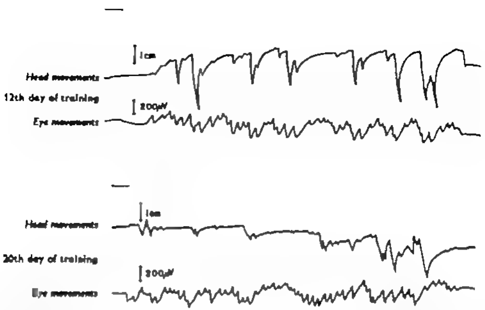

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Prior to training	to right	1st, sl	10, sm	32, sm
	to left	1st, sl	11, sm	31, sm
6th day of training	to right	1st, l	12, sm	46, sm
	to left	1st, l	20, sm	4[illegible], sm
12th day of training	to right	1st, m	18, l	41, m
	to left	1st, m	16, l	41, m
24th day of training	to right	1st→3rd, m	16, m	4[illegible], l
	to left	1st→3rd, m	18, m	43, l

Results obtained in the other experimental animals

The results obtained in the other guinea pigs, i.e. Nos. 2 and 3, are shown in Tables 1 and 2. The terms 1st, 2nd and 3rd position appearing in the table are defined as follows 1st position is that of the head deviating in the same direction as that of cylinder rotation 2nd position means the median position of the head. 3rd position is that of the head deviating opposite to cylinder rotation, or deviating so as to counteract the flow of the black lines of the optic cylinder

Thus, 1st → 3rd position, for example means that the head deviated in the same direction as that of cylinder rotation at an early period of optic stimulation, came to deviate in the direction opposite to cylinder rotation on further continuation of the stimulation As for the degree of the head deviation, "slight" deviation indicates the deviation within 1 cm from the base-line in the record, "medium" deviation indicates the one from 1 cm to 2 cm from the base line and "large" deviation means the one of more than 2 cm from the base line As for description of the head nystagmus, "small", "medium" and "large" are used "small" refers to the amplitude less than 1 cm in the record, "medium" to the one from 1 cm to 2 cm, and "large" to the one more than 2 cm respectively For the recording of the eye nystagmus, the apparatus was set in such a condition that the amplitude of standard calibration of 200 μV/sec was about 10 mm. Amplitude of the eye nystagmus was described as "small" (less than 3 mm) "medium" (from 3 mm to 6 mm) or "large" (more than 6 mm)

The results obtained in Nos. 2 and 3 showed some differences in detail from the result in No. 1 However it is worth noting that through optic training these cases also showed essentially the same type of modification of the optic reflexes as those observed in No. 1

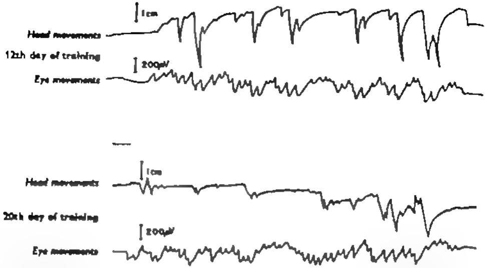

FIG. 2 Recordings of the head and the eye movements caused by optic stimulation after optic training The upper part of the figure indicates a recording of the head and the eye movements on the 12th day of the training, and the lower part the movements on the 20th day of the training In each part of the figure the upper line shows the head movements, and the lower the eye movements.

Fig 2 right rotation of the optic cylinder caused a distinct right deviation of the head The head nystagmus increased its amplitude markedly but rather reduced its frequency and showed 23 jerks in 40 seconds During the eye nystagmus to the left of increased amplitude we recorded 47 jerks in 40 seconds

Left rotation of the optic cylinder caused a marked left deviation of the head During the head nystagmus to the right of medium amplitude we noted 10 jerks in 40 seconds During the eye nystagmus to the right of medium amplitude we recorded 53 jerks in 40 seconds.

(iv) *On the 20th day of the training* As shown in the lower part of Fig 2 when the optic cylinder was rotated to the right the animal responded to this optic stimulation by turning its head moderately to the left and taking up the head position which seemed to counteract the flow of the black lines of the optic cylinder The head nystagmus to the left became smaller in amplitude and reduced in frequency and showed 21 jerks in 40 seconds However the eye nystagmus to the left was still of large amplitude and showed 50 jerks in 40 seconds

When the optic cylinder was rotated to the left the head deviated slightly to the left However as the optic stimulation was continued further the head of the animal turned to the right and took up the head position which seemed to counteract the flow of the black lines of the optic cylinder During the head nystagmus to the right of less amplitude we noted 4 jerks in 40 seconds During the eye nystagmus to the right of large amplitude we observed 52 jerks in 40 seconds

TABLE 1 *Changes in the optic reflexes induced by optic training (guinea-pig No 2)*

sm = small; l = slight m = medium l = large

Course of training	Direction of cylinder rotation	Head position, degree of deviation	Head nystagmus, frequency amplitude	Eye nystagmus, frequency amplitude
Prior to training	to right	1st, sl	10 sm	32, sm
	to left	1st, sl	11 sm	31 sm
6th day of training	to right	1st, l	12, sm	46, sm
	to left	1st, l	20 sm	45, sm
12th day of training	to right	1st, m	[illegible] l	41 m
	to left	1st, m	16, l	41 m
20th day of training	to right	1st→3rd, m	16, m	45, l
	to left	1st→3rd m	18, m	43, l

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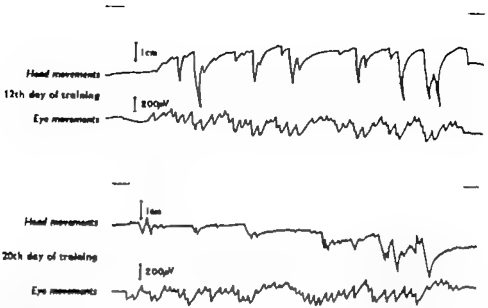

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(iv) *On the 20th day of the training* As shown in the lower part of Fig 2, when the optic cylinder was rotated to the right the animal responded to this optic stimulation by turning its head moderately to the left and taking up the head position which seemed to counteract the flow of the black lines of the optic cylinder The head nystagmus to the left became smaller in amplitude and reduced in frequency and showed 21 jerks in 40 seconds However the eye nystagmus to the left was still of large amplitude and showed 50 jerks in 40 seconds

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Prior to training	to right	1st, sl	10, sm	32, sm
	to left	1st, sl	11, sm	31, sm
6th day of training	to right	1st, l	12, sm	46, sm
	to left	1st, l	20, sm	45, sm
12th day of training	to right	1st, m	19, l	44, m
	to left	1st, m	16, l	41, m
20th day of training	to right	1st→3rd, m	16, m	45, l
	to left	1st→3rd, m	18, m	43, l

Results obtained in the other experimental animals

The results obtained in the other guinea pigs, i.e. Nos. 2 and 3, are shown in Tables 1 and 2. The terms 1st, 2nd and 3rd position appearing in the table are defined as follows 1st position is that of the head deviating in the same direction as that of cylinder rotation 2nd position means the median position of the head. 3rd position is that of the head deviating opposite to cylinder rotation, or deviating so as to counteract the flow of the black lines of the optic cylinder

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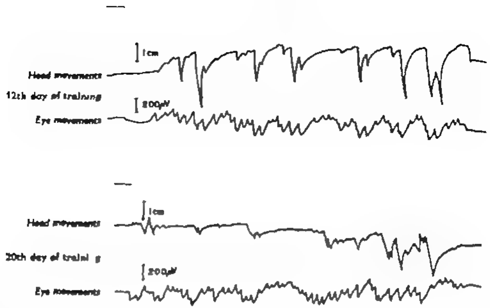

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Left rotation of the optic cylinder caused a marked left deviation of the head During the head nystagmus to the right of medium amplitude we noted 10 jerks in 40 seconds During the eye nystagmus to the right of medium amplitude we recorded 53 jerks in 40 seconds

(b) *On the 20th day of the training* As shown in the lower part of Fig 2, when the optic cylinder was rotated to the right the animal responded to this optic stimulation by turning its head moderately to the left and taking up the head position which seemed to counteract the flow of the black lines of the optic cylinder The head nystagmus to the left became smaller in amplitude and reduced in frequency and showed 21 jerks in 40 seconds However the eye nystagmus to the left was still of large amplitude and showed 50 jerks in 40 seconds

When the optic cylinder was rotated to the left the head deviated slightly to the left However as the optic stimulation was continued further the head of the animal turned to the right and took up the head position which seemed to counteract the flow of the black lines of the optic cylinder During the head nystagmus to the right of less amplitude we noted 4 jerks in 40 seconds During the eye nystagmus to the right of large amplitude we observed 52 jerks in 40 seconds

TABLE 1 *Changes in the optic reflexes induced by optic training (guinea-pig No 2)*

sm = small sl = slight; m = medium l = larg

Course of training	Direction of cylinder rotation	Head position, degree of deviation	Head nystagmus, frequency amplitude	Eye nystagmus, frequency amplitude
Prior to training	to right	1st, sl	10 sm	32, sm
	to left	1st, sl	11 sm	34 sm
6th day of training	to right	1st, l	12, sm	46, sm
	to left	1st l	20, sm	45, sm
12th day of training	to right	1st, m	18, l	44 m
	to left	1st, m	18, l	41 m
20th day of training	to right	1st→3rd, m	16, m	45, l
	to left	1st→3rd, m	18, m	43, l

Results obtained in the other experimental animals

The results obtained in the other guinea pigs, i.e. Nos. 2 and 3 are shown in Tables 1 and 2 The terms 1st, 2nd and 3rd position appearing in the table are defined as follows 1st position is that of the head deviating in the same direction as that of cylinder rotation 2nd position means the median position of the head 3rd position is that of the head deviating opposite to cylinder rotation, or deviating so as to counteract the flow of the black lines of the optic cylinder

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The results obtained in Nos. 2 and 3 showed some differences in detail from the result in No 1 However it is worth noting that through optic training these cases also showed essentially the same type of modifications of the optic reflexes as those observed in No 1

TABLE 2 *Changes in the optic reflexes induced by optic training (guinea pig No 3)*

Abbreviations as in Table 1

Course of training	Direction of cylin der rotation	Head position degree of deviation	Head nystagmus, frequency amplitude	Eye nystagmus, frequency amplitude
Prior t training	to right	1st, sl	2 sm	31 sm
	to left	1st sl	0	25, sm
6th day of training	to right	1st l	4 sm	33 sm
	to left	1st l	3 sm	49 sm
12th day of training	t right	1st, m	20 l	58, m
	t left	1st m	10 l	53, m
20th day of training	to right	1st→3rd, m	10 m	41 l
	to left	1st→3rd m	18 m	50, l

COMMENT

The essential parts of the results of our experiments are as follows

(i) In untrained animals the head movements and the eye movements could be elicited by optic stimulation but they were not so marked In the vast majority of the experimental cases, deviation of the head in the same direction as that of cylinder rotation was not observed markedly and the amplitude of the head nystagmus was very small The eye nystag mus was also very small in amplitude and very few in number These findings seem to indicate that the optic equilibrium function is poor in untrained animals

(ii) When optic stimulation was applied daily to the animal deviation *of the head in the direction of cylinder rotation became gradually manifest* The head nystagmus increased its amplitude and in most cases its fre- quency too In parallel with this, the eye nystagmus also increased its amplitude and frequency These findings suggest that the optic head nystagmus has a function to activate the occurrence of the optic eye nystagmus thus causing improvement of adaptability of the optic organ to optic stimulation

(iii) However when optic training was continued further deviation of the head in the direction of cylinder rotation gradually lessened and the head approached median position Furthermore in the majority of the experimental cases, it was found that the head of the animal came to deviate in the direction opposite to cylinder rotation thus taking up the head position suggestive of counteracting the flow of the black lines of the optic cylinder The head nystagmus at that time was of rather small amplitude and in most cases its frequency was reduced However the eye nystagmus appeared markedly There were some animals which did not clearly show the above described stages of development of adaptability

to optic stimulation However it is worthy of note that in all cases there could be observed a stage in which the optic head nystagmus appeared markedly thus activating the occurrence of the optic eye nystagmus.

The fact that daily application of a certain amount of optic stimuli to animals or optic training can induce modifications of the optic spinal reflexes in animals, was already reported by Fukuda & Hinoki (1957) According to them an untrained chicken was apt to lose its body equilibrium when optic stimulation was applied by means of rotation of an optic cylinder like the present one when optic stimulation was applied to a chicken, its head and neck deviated in the direction of cylinder rotation, followed by deviation of its trunk in the same direction. When stimulation was continued further the chicken was hardly able to maintain its standing posture and fell down in the direction of cylinder rotation. Thus marked ataxia of optic origin was noted to appear However when the same chicken was trained by daily application of a certain amount of optic stimuli, it gradually came hardly to show any ataxia and also to respond well to optic stimulation with brisk optic head nystagmus

Furthermore, it is worthy of note that with further progress of the training, the chicken's head and neck (in some cases even trunk) deviated in the direction opposite to cylinder rotation, taking up the posture suggestive of counteracting the flow of the black lines of the optic cylinder At this stage of the training, no ataxia of optic origin was produced by optic stimulation, not even by optic stimulation of fairly long continuation.

In addition to the investigation mentioned above Fukuda, Hinoki Tokita & Oku reported that when the same optic stimulation was applied daily to animals (rabbits and guinea pigs) the animals came to show a marked occurrence of the optic eye nystagmus and to be *capable of* responding to intense optic stimulation, to which they had previously been unable to respond well (Fukuda, Hinoki, Tokita & Oku, 1957) Fukuda named this phenomenon "the response increase in the optic eye nystagmus" as previously mentioned Naturally we can safely say *that this* phenomenon is just contrary to the response decline of the postrotatory and the caloric nystagmus, which has been discussed by many investigators (Dodge 1923 Hoshino & Fukuda, 1954 Aschan, 1954 Hood & Pfaltz, 1954 Fukuda, Hinoki & Tokita, 1958 Crampton, 1961 Fluur & Mendel, 1962)

In view of these facts, we *cannot* but conclude from the standpoint of body equilibrium that the optic eye nystagmus is quite different in nature from the postrotatory and the caloric nystagmus. The results of our investigations are well compatible with the findings of Fukuda and his collaborators. In the experiments by these investigators, however the head and the eye movement caused by optic stimulation were observed separately and they estimated the equilibrium function of the optic organ on the basis of either one of these two movements. However the body movements and the eye movements are considered to cooperate with each

other in maintaining body equilibrium of human subjects and animals. Therefore it has been hoped that the two kinds of movements should be recorded simultaneously and they should be studied together so that the changes in the optic reflexes induced by optic training can be studied more precisely We believe that our present investigation could have met this expectation fairly well

As mentioned above, the optic spinal reflexes, which can facilitate adaptation of the optic organ to strenuous changes of the environment, express themselves not only by the head nystagmus but also by other forms of reflexes For example deviation of the head in the direction of cylinder rotation becomes manifest as optic training proceeds, and at the same time the optic eye nystagmus increases its amplitude and frequency Furthermore, as optic training goes on further the head of the animal deviates in the direction opposite to cylinder rotation Under such condition, occurrence of the optic eye nystagmus is also facilitated These findings would indicate that these two head deviations are both equilibrium reflexes, and their physiological roles are common in promoting occurrence of the optic eye nystagmus so as to improve adaptability of the optic organ to optic stimulation Of course there are considerable differences between the two head deviations mentioned above from the standpoint of body equilibrium Of various types of optic spinal reflexes, which appear through optic training the optic head nystagmus is of particular interest in that it can activate the optic eye nystagmus increasing its amplitude most strikingly Thus, it is permissible to conclude that the optic head nystagmus is a kind of equilibrium reflex and its physiological role is considered to promote the appearance of the optic eye nystagmus in order to enhance the function of the optic organ and subsequently to adapt the individual smoothly to strenuous changes of the environment in case where the individual is exposed to such intense environmental changes that the optic organ alone cannot react

This conclusion is supported by the fact that when the head of the animal which had been trained until marked head and eye nystagmus came to be elicited was fixed to its trunk together with its extremities, and thus the occurrence of the head nystagmus was inhibited the appearance of the optic eye nystagmus was also remarkably inhibited

Incidentally based on our experiments hitherto made we would like to comment here that the effects of training mentioned above are considered to be established by the formation of new optic equilibrium reflexes of a higher order in the extrapyramidal system as a result of repetitive application of optic stimulation i e optic training (Fukuda & Hinoki 1957) and that through optic training the proprioceptors in the neck regions, especially those in the deep group of the nuchal muscles can contribute considerably to the formation of the optic reflexes mentioned above in cooperation with the optic organ (Hinoki Terayama & Kashiwabara, 1965)

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The authors wish to express their deep gratitude to Dr K Sakata and Mrs. K. Mihara for th ir kind assistance in composing the English tran lation of this paper

ZUSAMMENFASSUNG

Drei erwachsene Meerschw inch n wurden täglich einem bestimmten Quantum optischer R ize ausgesetzt und daran gewöhnt. Das Resultat dieser Experimente machte klar dass durch die Wiederholung der optischen Reizung Formen der optisch-spinalen und optisch-okulären Refle e geändert wurden so dass sie die Anpassungsfähigk it der Individ en an die optische Reizung verbessern. Ebenfall wurde klar dass der optische Kopfnystagmus, de auf einer gewissen Stufe der ptischen Trainierung merklich auftrat, die Funktion hatt das Auftreten les optischen Augennystagmu zu intensivieren Auf Grund dieser Beobachtungen lässt sich f lgern dass di physiologisch R lle des optischen Kopfnystagmus darin besteht, die Funktion des optischen Organ zu unterstützen und weiterhin die Anpassung der I dividuen an eine beschwerliche Veränderung der Umgebung zu erleichtern f lls ei Individuum so intensiven Umgebungsver nderungen usgesetzt ist, dass das optische Organ ll in le nicht bewältigen kann

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A COMPARISON OF NYSTAGMUS HABITUATION IN THE CAT AND THE DOG

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Dogs demonstrate declines in vestibular nystagmus as a function of repeated angular accelerations. The declines are relatively specific to a practised direction of response and only partial recovery occurs after one week of rest. The nystagmus modifications found in dogs are of the same general nature and of the same relative magnitude as those exhibited by cats similarly stimulated. Dogs, however, appear to show more voluntary eye movement during test procedures than do cats.

A response decline (habituation) of nystagmic eye movements resulting from repeated vestibular stimulation in the laboratory has been reported for a number of infra-human species. Thus birds (e.g. King, 1926; Fukuda, Hinoki & Tokita, 1958), white rats (Griffith, 1920), rabbits (e.g. Hood & Pfaltz, 1954) and cats (e.g. Crampton, 1962; Collins, 1964) all demonstrate a decline in vestibulo-ocular activity during a series of rotatory stimulations. The present paper seeks to extend knowledge of the effects of repeated vestibular stimulation to the canine species and to compare results from the dog with those of the cat. (The experiments reported herein were conducted according to the "Principles of Laboratory Animal Care" established by the National Society for Medical Research.)

METHOD

Apparatus

The Huffman Rotation Device (Collins & Huffman, 1964) was used to produce angular accelerations. The device was located in a light-proof room and was equipped with a pair of tiers so that three animals could be rotated at the same time with the heads of each located at the center of rotation (see Fig. 1).

Restraint

Restraint was effected by the method of Henriksson, Fernández & Kohut (1961) and in the manner noted elsewhere (Collins, 1964). For testing, each animal was wrapped in a towel and placed in a restraint box. Since the same boxes were used for both dogs and cats, only small, terrier type dogs were used.

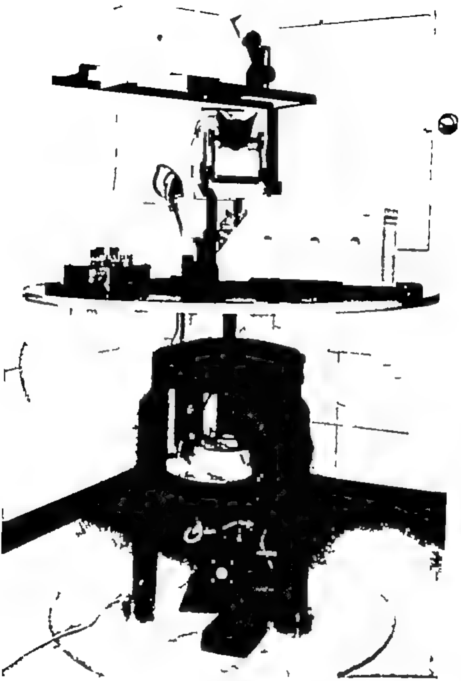

FIG. 1. Th Huffm n Rot t D ce with three Im l m nted l test po ll

Recording

Horizontal components of eye movements were recorded by means of needle electrodes inserted by the outer canthi. The recorder was an Offner Type R Dynograph with 3-sec time constants used in amplification. (On several occasions DC recordings were obtained from the d gs with no special preparation and using ordinary needle electrode. Such records were obtained for an entire session from 3 dogs with little or no drift of

TABLE 1. *The test sequence employed*

Pretests, habituation trials, and Post 1 tests were administered consecutively during a single day. Post 2 tests were given one week later. CW and CCW refer to clockwise and counterclockwise rotation, respectively. All trials consisted of 5°/sec² angular acceleration for 18 sec, 2 min of constant velocity and 0.15°/sec² angular deceleration

	Dogs		Cats	
	1–5	6–10	120–124	125–129
Pretests				
1	CW	CCW	CW	CCW
2	CCW	CW	CCW	CW
Habituation (15 trials)	CCW	CCW	CW	CW
Post 1 Tests				
1	CW	CCW	CW	CCW
2	CCW	CW	CCW	CW
Post 2 Test (1 week later)				
1	CW	CCW	CW	CCW
2	CCW	CW	CCW	CW
3	CW	CCW	CW	CCW
4	CCW	CW	CCW	CW

the recording pens. DC records were never obtained from the cats due to persistent drift problems.)

Prior to testing, animals were placed in an opto-kinetic stimulator. Horizontal eye movement calibrations were obtained at a drum speed of 24°/sec.

Procedure

The group of cats and the group of dogs each consisted of 10 animals. Both groups received 2 pretests, 15 habituation trials, and 2 posttests (Post 1) in a single day; one week later an additional 4 posttests (Post 2) were administered (see Table 1). In both groups, half of the animals received CW rotation on (*a*) the first pretest, (*b*) the first Post 1 test, and (*c*) the first and third Post 2 tests. CCW rotation occurred on (*a*) the second pretest, (*b*) the second Post 1 test, and (*c*) the second and fourth Post 2 tests. For the remaining 5 animals in each group, the order of presentation of the CW and CCW trials was reversed. Habituation trials were all CCW for the dogs and all CW for the cats. Each trial consisted of an angular acceleration (5°/sec² for 18 sec), a 2 minute period of constant velocity (at 15 rpm) and a sub-threshold deceleration (0.15°/sec² for 600 sec) to zero velocity. Rest periods between successive trials were 3 minutes in illumination. The trials themselves were conducted in total darkness. None of the animals had been used in previous experiments.

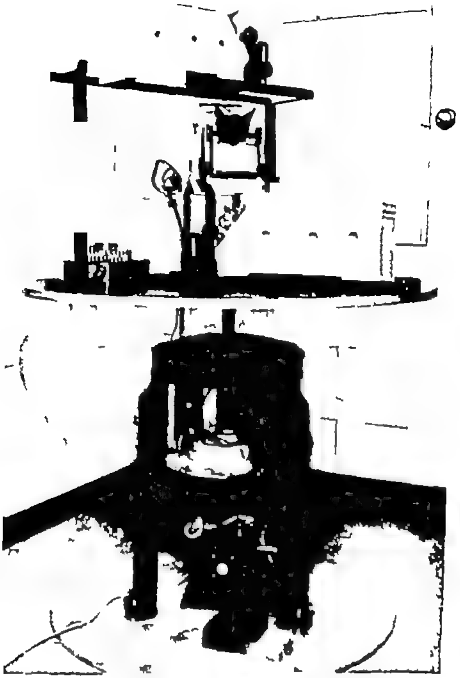

Fig. 1 The Hoffman Rotation Device with three animals mounted in test position

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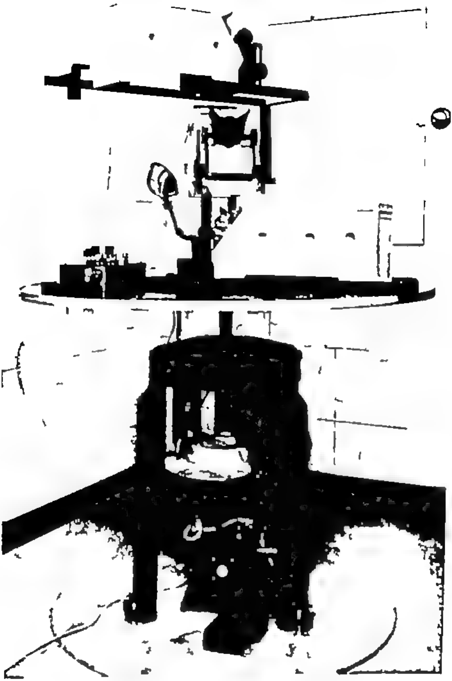
Prior to testing, animals were placed in an opto-kinetic stimulator. Horizontal eye movement calibrations were obtained at a drum speed of 4°/sec.

Procedure

The group of cats and the group of dogs each consisted of 10 animals. Both groups received 2 pretests, 15 habituation trials, and 2 posttests (Post 1) in a single day; one week later an additional 4 posttests (Post 2) were administered (see Table 1). In both groups, half of the animals received CW rotation on (*a*) the first pretest, (*b*) the first Post 1 test, and (*c*) the first and third Post 2 tests. CCW rotation occurred on (*a*) the second pretest, (*b*) the second Post 1 test, and (*c*) the second and fourth Post 2 tests. For the remaining 5 animals in each group, the order of presentation of the CW and CCW trials was reversed. Habituation trials were all CCW for the dogs and all CW for the cats. Each trial consisted of an angular acceleration (5°/sec² for 18 sec), a 2 minute period of constant velocity (±15 rpm) and a sub-threshold deceleration (0.15°/sec² for 600 sec) to zero velocity. Rest periods between successive trials were 3 minutes in illumination. The trials themselves were conducted in total darkness. None of the animals had been used in previous experiments.



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2	CCW	CW	CCW	CW
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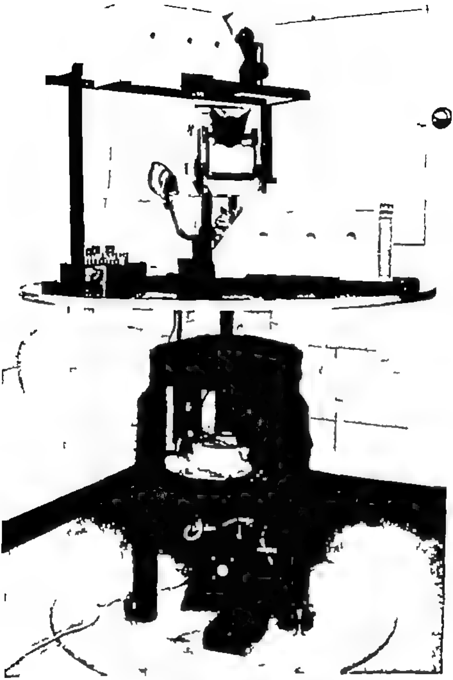

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only less than for the practiced direction for both types of animals, but were also proportionately alike for the two groups.

For both groups of animals the habituated direction of response exhibited recovery after a one-week rest period Recovery however was not complete

Time-course plots of primary and secondary slow-phase activity for habituation trials 1 5 10 and 15 appear in Fig 5 The overall depression of primary activity from trial 1 to trial 5 is relatively more pronounced for the group of dogs. In addition, secondary nystagmus from the dogs decayed quickly without showing the rise and decline which seem to characterize the secondary response of the cats however this may be due partly at least to the fact that a considerable number of voluntary eye movements by the dogs made scoring of the secondary responses difficult

Although the group of cats yielded considerably more slow phase displacement and a greater number of nystagmic eye movements than did the dogs, generalizations concerning inter species differences in magnitude of response are not appropriate with samples of this size. Differences in nystagmus output among similar-size groups of the same species are frequently of this magnitude.

ACKNOWLEDGMENT

W gratefully ack wledge assistan rendered by T rea Lee and Joseph E. Duchon

RESUME

Les hien montrent des diminutions du nystagmus estibulaire par suite des accélération gulaires repétées. Ces dimin tions sont relativement spécifique à un côté exercé de répo se et une rétablissement seulement partielle se produit près un sem le sans stimulati n Les modifications de nystagmus qui se trouvent aux chiens sont du même genre général et de la mêm grandeur rélative que celles qu se font voir aux chats qui f rent stimulés d une manière semblable Les ch ens, cependant semblent d montrer plus d mouvements volontaires des yeux pendant le procédé d recherche qu ne m ntrent les chats d une ituation semblable

ZUSAMMENFASSUNG

Hund weisen Abschwächungen des vestibulären Nystagmus infolge wiederholter ngulärer Beschleunigungen auf Die Abschwächungen ind erhältnismässig spezifisch fur ine gewöhnte Reakti srichtung, und ein nur un oll-stä d ge Reaktionswiedergewinnu g kommt n ch einer Woche ohne R izung vor Die Nystagmus eränderungen bei Hunden sind von gleicher allgemeiner Beschaffenhe t und gleicher relativer Grösse wie bei uf ähnliche Weise angereizten K t en. Hund haben jedoch anscheinend ein willkü lichere Augenbewegung während des U tersuchungsvorgangs als K tzen

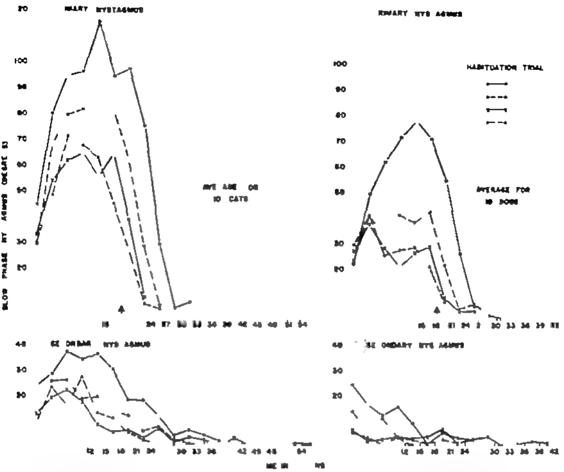

FIG. 5 Time-course plots of dog and cat slow ph se eye displacement during h bituati n trial 1 5, 10 and 15 Arrows indicate the point f stimulu termination in the "Primary Nystagmus pl ts "Second ry Nystagmu urves are plotted with an rbitrary zero time as though ea h urve began at the sam poi t in time (secondary responses actually appear ea lier with repeated t i ls) N te that habituati n t i l 1 is n t the first act al trial for that stimulu directi one of th Pre-tests was identi al t the habituati n tri ls.

animals a fairly steady trial to-trial decline occurred in the practiced direction for the 3 response measures, with duration of nystagmus showing the shallowest slope The percentage of response decline for each measure was quite similar for the two groups Thus, for the dogs, duration declined 33 1% number of nystagmic beats 55% and slow phase nystagmus 77.2% for the cats response declines for these same measures were 32 0% 55 1% and 68 7% respectively

Habituation of nystagmus was relatively specific to the practiced direction Thus, for the dogs the pre to posttest declines for the unpracticed direction of nystagmus were only 10.5% in duration, 21.2% in number of beats and 48 7% in slow phase displacement For the group of cats, the same measures declined 16 1% 23 4% and 45.5 respectively Thus changes in nystagmus production in the unpracticed direction were not

only less than for the practiced direction for both types of animals, but were also proportionately alike for the two groups.

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RÉSUMÉ

Les hien montrent des diminutions du nystagmus vestibulaire par suite des accélérations ngulaires repétées. Ces diminuti ns sont relativement spécifique à un côté exercé d réponse et un rétablissement seulement partielle se produit près une sem in sans stimulation Les modifications d nystagmus qui se trouvent aux chiens sont du même genre général et de la même grandeur rélative que celles qui se f nt voir aux chat qui furent stimulés d'un manière semblable Les chiens, cependant semblent de montrer plus de mouvements volontaires des yeu penda t le procédé de recherche que n montrent les chats dans un situation semblable

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Receiv d December 21 1965

INDICATIONS FOR ESOPHAGEAL RECONSTRUCTION OF CORROSIVE STRICTURES

R. HÄRMÄ and L. W. F. LINDEX
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From the Central Hospital of Kuopio

The principal indication for operation is an old stricture that has caused dysphagia and cannot be dilated with sounds greater than 30–33 Charrière. Cases involving severe complications owing to perforation also call for reconstructive surgery. Psychological disturbances caused by constant repetition of treatment add to the indications for operation as does an imminent danger of carcinoma. Short strictures can be treated with local surgery, longer ones call for total reconstruction of the esophagus. Five cases are presented and the methods of reconstruction discussed.

Severe strictures resulting from esophageal corrosions have become considerably less numerous in recent years. This is due partly to improved treatment and partly to a reduction in the use of lye for laundry. Their frequency has been further reduced by administering antibiotics and cortisone in fresh cases. But there are still some patients whose treatment for strictures was originally ineffectual or has been completely neglected. Not even modern antibiotics and cortisone are able to prevent strictures from forming in deep corrosions.

The majority of strictures of the esophagus can be treated with dilatative soundings, but it is downright dangerous to treat long-neglected strictures by mere conservative methods. Kivirenta (1949) writes as follows: "If there is stenosis, complications frequently appear during the treatment. In these cases, mortality was 32 per cent (49/155). The local end result was good in 0 per cent of the cases that survived (84/106), but this required an average of 31.8 ± 4.8 months' treatment."

Appelberg (1960) made follow-up examinations of 111 corrosions treated during the last ten years; the results had been good in 86.5% of the cases, fair in 11.7% and poor in two cases. Shertsov (1962) reached practically the same conclusion: out of 225 cases, 70.2% were good, 23% fair and 2.6% poor. Plastic surgery was performed in the latter cases.

If a stricture appears during or after the primary corrosion treatment, it often becomes chronic and dilatation gives only temporary relief. In the worst cases the patients must be sounded repeatedly for months on end, or for the rest of their lives. Soundings may involve certain dangers. Ungerecht (1963) lists the most important of these: (1) fever, probably

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Fig. 1 Constricted esophag and the retrosternal colon transplant i case 1

It was easy to dilatate and had been repeatedly dilatated by bouginage to 4 Charrière fo 1 / years, but th dysphagia always ret rned 2–3 week late Biopsy f the granulating ti sue revealed unspecific inflammation Th patient h d lost weight and w afflicted psychologically

Her colo was sterilized with succinyl-sulphathi trol and neomy in, and emptied. A colon tra position was performed retrosternally from the neck to the stoma h using a long transplant from the transverse and descending colon. The ascending colo was anastomosed to the sigm id. The patient recovered without complicati ns. After surgery sh could eat freely and a X-ray con firmed th t her food passage wa good A follow-up 2 years later showed an 18 kg increase in weight and good passage of food

Comment A case of esophageal stricture in l ing nutritional disorders which called for repeated dilatation at short intervals. Granulating tissue in th esophagus, caused by chronic inflammation, implied a da ger f carcin ma Th esophagu wa reconstructed by mean of colon transpositio fter which her nutrition and food passage became good.

Case 2

Th patient, 20-year-old working man had drunk ly 17 years previously His esophageal stricture had been treated by dilatati n 7 years ea lier he had n dergone gastric resection f stomach ulcer 3 weeks fter this he had been operated f leal strangulatio and 60 cm of hi ileum h d been resected

Using esophagoscopy we diagnosed long stricture in the upper middle part f th esophagus. Th stricture could only be dilated to 27 Charrière, and the patie t was suffering from dysphagia Bougin ge caused a perforation in the

due to the spread of the infection (2) paraesophageal inflammations, *possibly without perforation* (3) hemorrhages, though these are generally slight (4) perforation of the esophagus, which leads to mediastinitis, pleuritis pericarditis peritonitis tracheobronchial fistulas, and perforations of the major blood vessels.

Esophagitis appears at and above the point of the stricture owing to the retention of food In many cases this leads to carcinoma within 20–30 years

Reconstructive surgery of the esophagus has been developed in recent years and has produced satisfactory results It is employed for severe strictures Unfortunately there is a certain lack of agreement regarding its indications Ungerecht is opposed to radical innovations He feels that surgery should come into play only after all the conservative methods have been tried out He considers that it is indicated if soundings taken after primary treatment reveal obstructions of an anatomical nature (bends and sacs in the esophagus) Owing to the eventual danger of carcinoma surgery is more justifiable for young patients.

The formulation of operative indications depends partly on the reliability of the method as measured by mortality Various statistics give mortality as 2–5% when total reconstruction, using the colon is performed in one or two phases. This is borne out by our own findings We favour reconstructive surgery if any of the following combinations of symptoms are noted

(1) The esophageal stricture prevents the passage of food and hampers the patient s normal nutrition The stricture is chronic and has to be dilatated repeatedly at short intervals (2 weeks to 2 months) and does not admit sounds larger than 30–33 Charrière Soundings create a constant risk of complications, particularly perforation There is inflammation in the esophagus which seems likely to turn into carcinoma later on Naturally these symptoms include cases in which the esophagus does not admit any sound of sufficient size, and the patient has to be *fed by gastrostomy*

(2) Dilatation has caused an anatomical obstruction or perforation through a *rupture at the point of the stricture* with consequent disorders.

(3) Repeated dilatation is leading to psychological disorders (in the case of children)

(4) The strictures are short and isolated and can be removed by local plastic surgery

Here are some cases in which the above indications for operation have been applied

Case 1

The patient a 17 year-old girl had probably swallowed lye as a child and *received no treatment* at the time Later dysphagia developed and endoscopical examination revealed a granulating stricture in the upper third of the esophagus

Fig. 1 Constricted esophagu nd the retrosternal colo transplant in case 1

It was easy to dilatat and had been repeatedly dilatated by bouginage to 45 Charrière f 1 years, but the dysphagia alway returned 2–3 weeks later. Biop y of the granulating ti sue revealed unspecifi inflammation. The patient had lost weight d was afflicted psychologically.

Her colon was sterilized with succi yl-sulphathiatzole and eomycin, and emptied. A colon *transposition* was perf rmed retrosternally from the neck to the stomach using *a long transplant from the transverse* and descending colon. Th scending colon wa anastomosed *to the sigm id. Th* patient recovered without complications. After *surgery she could* eat freely and an X-ray con f rmed that her *food passage was good. A follow-up 2 years later* showed n 18 kg increase in weight and good pa sage of food.

Comment. A case of esophageal stricture involving *nutritional disord rs* which called for repeated dilatation at short i tervals. *Granulating tissue* in the esophagus, caused by chroni inflammati n implied a da ger of carcinoma. The esophagus was reconstructed by means of colon transposition, after which her trit on and food passage became good.

Case 2

The patient, a *39-year-old* working man had drunk ly 17 years previously. His esophageal tricture had been *treated by dilatation* 7 years earlier he had u dergone gastric resection f a *stomach* ulcer 3 weeks fter thi he had been operated for ileal stra gulation and 60 cm *of his* ileum had been resected.

Using esophagoscopy we d gnosed *a long stricture* in the upper middle part of the esophagus. The stricture could only be dilated to 27 Charrière and the patient was *suffering* from dysphagia. Bouginage caused a perforation in the

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THE EFFECT OF TRAUMA IN CAUSING COCHLEAR LOSSES AFTER STAPEDECTOMY

M. M. PAPARELLA
Columbus Ohio U.S.A

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Trauma undoubtedly may play an important role in causing sensori neural deafness after stapedectomy I stapedectomy trauma may be considered indirect (stimulation of the intact ossicles) r direct (disturbance f the estibular cont t) In evaluating indirect trauma the ossicula chain was stimulated in trained cat resulting in acoustic trauma lesions of the basal turn Direct trauma was evaluated by making sac cula lesions through the oval window in the squirrel monk y and cat. Thi resulted in normal cochlear findings. These findings indicate that acousti trauma more likely result from a massi e v lume displacement of perilymph beneath an intact footplate. Alth ugh trauma sometimes xplain severe cochlear deafness immediately following stapedectomy it does not explain the delayed deafness which may follow an initial good result.

It is known that manipulation or instrumentation of the ossicles may produce high frequency hearing losses in almost any type of reconstructive middle ear surgery This has been demonstrated in mastoidectomy reconstruction for congenital atresia, stapes mobilization and stapedectomy (Schuknecht & Tonndorf 1960 Paparella, 1962)

Trauma undoubtedly plays an important role in causing sensorineural deafness after stapedectomy There is a significantly greater incidence of cochlear losses following drilling and removal of the footplate in obliterative otosci rosis. Shambaugh (1962) reports that 82.5% of cochlear losses after t pedectomy had markedly thickened footplates.

Acoustic trauma has been experimentally seen as a result of stimulating the os icles with the bone cutting bur Using behaviorally conditioned cats a larger cutting bur (4 mm) was found to be more damaging to the basal turn than the maller cutting bur (1.2 mm) (Paparella, 1962) The larger bur transmits a greater amplitude of motion to the stimulated ossicle

This investigation w supported in part by Public Health Service Grant Number NB 04720-01 nd by the General Research S pport Grant of the United States Public Health Service

ZUSAMMENFASSUNG

Alte Strikturen die Dysphagie verursacht haben und beschwerlich oder un möglich mit grösseren Bougiegrössen als 30–35 Charrière zu bougieren sind machen die wichtigste Indikation für die rekonstruktive Ösophaguschirurgie aus. Die Fälle mit schweren Komplikationen infolge einer Perforation sind auch mit rekonstruktiver Chirurgie zu behandeln Sowohl die von einer endlos wieder holten Bougierung herrührenden psychologischen Störungen als auch drohende Kanzerisierung verstärken die Indikationen für eine Operation Kurze Strikturen kann man mit lokalen chirurgischen Massnahmen behandeln die längeren Strik turen erfordern eine vollständige Rekonstruktion des Ösophagus. Nach einer Dar stellung von fünf Fällen werden die Methoden der Rekonstruktion besprochen

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FIG. 2. Saccular w ll lesion which w made with needle through an i tact footplat how healing and fixation of the saccular wall t the footplate. Not osteogenesis of the footplat to mal in 2 a. The macula nd cochlea is normal in such animal.

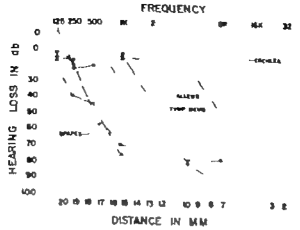


FIG. 1 A

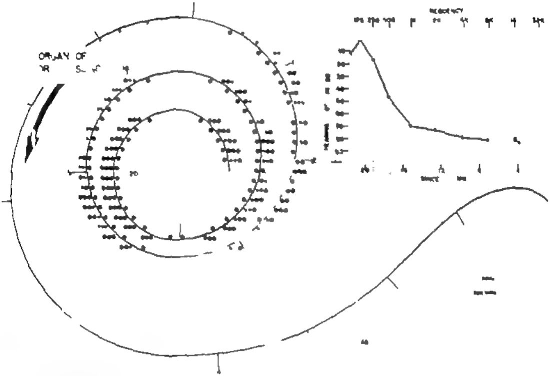


FIG. 1 B

FIG. 1 (*A*) Compo it udiograms of ll an mal receivi g timul ti n with the high frequency microvibrat Cochl capsule t mulation for three minut re ulted in high frequ ney hearing l al n M ll stimul ti n f twe t thirty nd i ty second resulted in proportionat ly greater hearing l ses St pes timul tion f t seco d caused the gr test hea i g loss. (*B*) Cat 5 Cocl le r graphic reco tructi nd audiogram f cat recei ing t n secon l timul ti n t tapes Creat t d m g l i tl e lowe basal turn with h ir cell dam g i ll three turns.

which probably results in a greater volume displacement of perilymph beneath the footplate

In cats behaviorally conditioned to obtain audiograms it was further found that stimulating the ossicles with a high frequency microvibrator similarly produced acoustic trauma lesions of the basal turn (Laparella

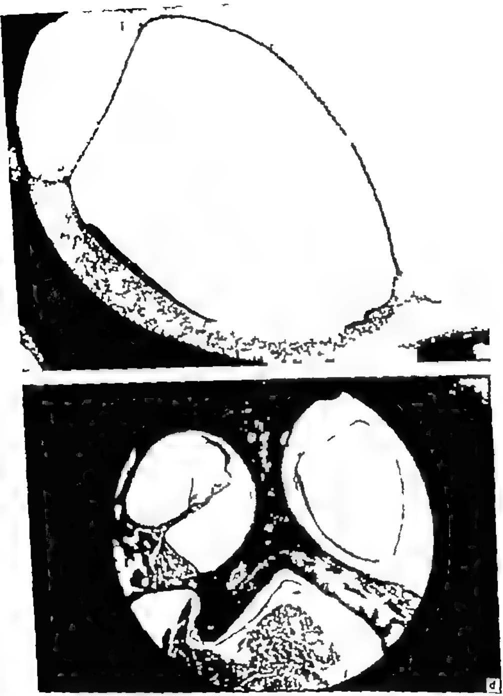
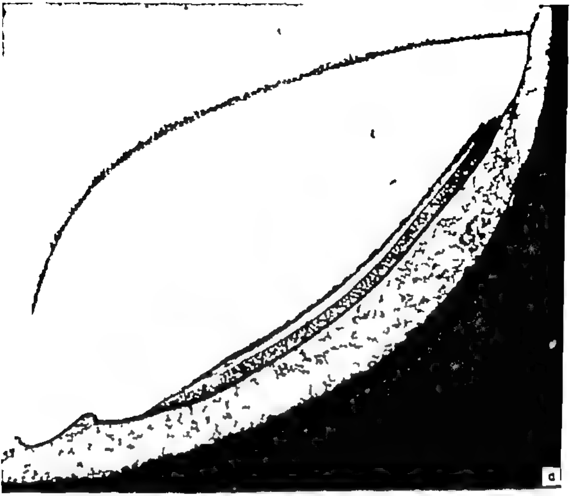


Fig. 3 (Normal monkey saccule for comparison. (*b*) The saccular wall defect which was made in this animal did not heal. There is degeneration of the otolithic membrane of the macula which otherwise appears normal. ( ) There is complete absence of the otolithic membrane and degeneration of the neuroepithelium of the macula. The defect in the saccular wall has healed. (*d*) This shows the saccular lesion and the normal organ of Corti of the adjacent basal turn in the same monkey 3. The rest of the cochlea was entirely normal.



brane is missing and there is hydrops of the saccule and scala media. The saccule wall is attached to the oval window graft of adipose tissue. (*d*) This saccule wall has attached itself to the oval window graft and the otolithic membrane is missing. The normal organ of Corti in the basal turn adjacent to the saccule is seen.

FIG 4 (*a*) The epithelium f the m cula ppears n rmal b t the t toco l are mi ing The accular wall ha healed against the al wind w graft f dipos tis ue At another lev l in thi ear tl fibrou oval window g ft l d nt th saccul r w ll Not normal cochlea (*b*) Th saccul r w ll ha healed lo g the path f the needl The statoconia re di rupted but the inne ear i therwise n rm l ( ) The ot lithi mem

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FIG. 3. The entire stapes is seen within the vestibule compressing the saccular wall w ll the utricle. There is slight disruption of statoconia in the saccule. The cochlea is normal. The plastic graft i seen bet the fibrous tissue filling the oval window

Two of the seven monkey stapedectomy ears developed suppurative labyrinthitis from contamination either during or subsequent to surgery. The remaining five ears demonstrated various saccular lesions classified from mild to severe as follows. (1) Saccular wall lesion alone with adhesion formation to the oval window graft. (2) Disturbance of the otolithic membrane. (3) Complete degeneration of the otolithic membrane. (4) Degeneration of the neuroepithelium of the macula. (Figs. 3 and 4)

The cat ears showed macular degeneration without other vestibular or cochlear findings. It was surprising that in spite of exaggerated attempts at mechanical destruction histological evidence of saccular damage was much less than anticipated.

The organs of Corti were examined by serial sections in all animals and were norm l. The cochlea were otherwise entirely uninvolved with the exception of one monkey ear which had moderate hydrops.

DISCUSSION

In spite of exaggerated attempts at saccular destruction in the cat or monkey the cochlea may appear normal and the saccular lesion may appear much less severe than anticipated with healing of the saccular wall. This same general finding was made by Igarashi (1965) in monkeys.

1961) A shorter period of stimulation to the stapes resulted in greater damage to the organ of Corti than longer stimulation to the tympanic membrane and malleus (Fig 1)

A lesion restricted to the upper basal turn corresponding to the 4000 cycles per second region can also result from experimental stapes fractures in cats (Singleton & Schuknecht 1959) The progression of audiometric change and the extent and location of histopathology was evaluated in stimulation deafness in humans and animals It was seen that damage from acoustic trauma extended along the cochlear partition more rapidly in a basal than in an apical direction The explanation for this was based on the traveling wave phenomenon of Békésy (Paparella & Melnick in press)

With the above experimental findings we see that mechanical stimulations through the intact ossicles may produce volume displacements beneath the stapes footplate resulting in typical acoustic trauma lesions of the basal turn It is of interest to consider the possibility of cochlear damage in *direct mechanical trauma to the vestibular contents during stapedectomy*

In the monkey as in man the saccule is more susceptible to direct traumatic lesions than the utricle which is more superiorly located and *partially protected by the horizontal portion of the facial nerve* We produced saccular lesions during stapedectomy in seven squirrel monkey ears In two other squirrel monkey ears a saccular lesion was attempted through an intact footplate These monkeys were from a larger group in which stapedectomy was combined with experimental tympanoplasty (Paparella in press) Saccular lesions were also made in two cats through a stapedectomy approach

METHOD

In each case the animal was anesthetized with intraperitoneal sodium pentobarbitol and the stapes exposed using a trans canal approach after elevating a tympano meatal flap A posterior superior auricular approach was used for the cat The stapes bone was usually removed atraumatically in one piece The macula of the saccule was easily *identified and a straight* needle was used to disrupt the macula The oval windows in these ears were not enlarged by drilling Either gel foam or autogenous adipose tissue *was used as the oval window graft*

RESULTS

These animals had an unremarkable post-operative recovery the same as animals having stapedectomy alone and showed no significant vestibular findings

Attempting a blind saccular lesion *through an intact footplate* resulted in a saccular wall lesion alone with healing and fixation to the stapes footplate (Fig 2)

Fig. 5. The entire stapes is seen within the vestibule compressing the saccular wall as well as the utricle. There is slight disruption of statoconia in the saccule. The cochlea is normal. The silastic graft is seen above the fibrous tissue filling the oval window

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In performing stapedectomy surgery in humans rarely a fragment of the stapes may drop into the vestibule or even more rarely the tip of a hook used in removing the footplate may inadvertently break off and fall into the inner ear Although this technical complication is totally preventable and should never occur the patient may recover uneventfully and have an excellent hearing result post-operatively in spite of a foreign body present within the inner ear and great consternation on the part of the otologist

In another monkey ear from a separate study the stapes was pushed into the vestibule and a silastic graft positioned above this (Paparella & Saunders) In this ear the entire stapes is seen within the vestibule pushing upon the saccular and utricular wall There is only a mild disturbance of the statoconia of the saccule and the cochlea is entirely normal (Fig 5)

Although all forms of trauma during stapes surgery are to be avoided it would appear that indirect trauma through an intact footplate may more likely produce acoustic trauma lesions of the basal turn of the cochlea than inadvertent direct trauma to the saccule This observation has also been made clinically (Lewis 1961)

Lawrence, Wolsk & McCabe (1961) and Schuknecht (1953) have shown that direct cochlear mechanical lesions may be made with the resulting pathology being restricted to the site of injury Adjacent areas of the cochlea were found to be normal histologically and functionally It should therefore not be surprising that damage to the otolithic organs might likewise result in normal cochlear findings. Of course vestibular symptoms due to disturbance of the otolithic organs may occur

There are many other factors which together with trauma may produce sensorineural deafness after stapedectomy such as toxicity infection, and hypersensitivity It would seem that the effects of trauma in producing cochlear deafness should be observed soon after stapedectomy This does not account for the delayed severe sensorineural deafness which may sometimes follow an uncomplicated stapedectomy procedure

ZUSAMMENFASSUNG

Stapedektomie spielt zweifellos eine wichtige Rolle in der Verursachung von Nervenschwerhorigkeit Trauma bei Stapedektomie kann auf zwei Arten erfolgen Auf indirektem Wege durch die Stimulation der intakten Gehörknöchelchenbrücke oder auf direktem Wege durch Störung des vestibularen Inhalts. Um das direkte Trauma beurteilen zu können wurde die Gehörknöchelchenkette von Versuchskatzen stimuliert und das Resultat war eine akustische Traumalasion in der basalen Schneckenwindung Direktes Trauma wurde beurteilt indem durch das ovale Fenster Läsionen im Sacculus von Affen und Katzen erzeugt wurden. Hier waren die cochlearen Befunde normal Die Ergebnisse zeigen dass akustisches Trauma wahrscheinlich mehr durch eine massive Volumenverdrängung von Perilymphe unterhalb einer intakten Fussplatte erzeugt wird Dieses erklärt

die gelegentlich schwere cochleare Schwerhörigkeit, die sofort einer Staped ektomie f lgt. E erklärt jedoch nicht die verspätet Schwerhörigkeit, die einem ursprünglich guten Resultat folgt.

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In performing stapedectomy surgery in humans rarely a fragment of the stapes may drop into the vestibule or even more rarely the tip of a hook used in removing the footplate may inadvertently break off and fall into the inner ear Although this technical complication is totally preventable and should never occur the patient may recover uneventfully and have an excellent hearing result post-operatively in spite of a foreign body present within the inner ear and great consternation on the part of the otologist

In another monkey ear from a separate study the stapes was pushed into the vestibule and a silastic graft positioned above this (Paparella & Saunders) In this ear the entire stapes is seen within the vestibule pushing upon the saccular and utricular wall There is only a mild disturbance of the statoconia of the saccule and the cochlea is entirely normal (Fig 5)

Although all forms of trauma during stapes surgery are to be avoided it would appear that indirect trauma through an intact footplate may more likely produce acoustic trauma lesions of the basal turn of the cochlea than inadvertent direct trauma to the saccule This observation has also been made clinically (Lewis, 1961)

Lawrence Wolsk & McCabe (1961) and Schuknecht (1953) have shown that direct cochlear mechanical lesions may be made with the resulting pathology being restricted to the site of injury Adjacent areas of the cochlea were found to be normal histologically and functionally It should therefore not be surprising that damage to the otolithic organs might likewise result in normal cochlear findings Of course vestibular symptoms due to disturbance of the otolithic organs may occur

There are many other factors which together with trauma may produce sensorineural deafness after stapedectomy such as toxicity infection, and hypersensitivity It would seem that the effects of trauma in producing cochlear deafness should be observed soon after stapedectomy This does not account for the delayed severe sensorineural deafness which may sometimes follow an uncomplicated stapedectomy procedure

ZUSAMMENFASSUNG

Stapedektomie spielt zweifellos eine wichtige Rolle in der Verursachung von Nervenschwerhörigkeit Trauma bei Stapedektomie kann auf zwei Arten erfolgen Auf indirektem Wege durch die Stimulation der intakten Gehörknöchelchenbrücke oder auf direktem Wege durch Störung des vestibulären Inhalts. Um das direkte Trauma beurteilen zu können wurde die Gehörknöchelchenkette von Versuchskatzen stimuliert und das Resultat war eine akustische Traumaläsion in der basalen Schneckenwindung. Direktes Trauma wurde beurteilt indem durch das ovale Fenster Läsionen im Sacculus von Affen und Katzen erzeugt wurden Hier waren die cochlearen Befunde normal Die Ergebnisse zeigen dass akustisches Trauma wahrscheinlich mehr durch eine massive Volumenverdrängung von Perilymphe unterhalb einer intakten Fussplatte erzeugt wird Dieses erklärt

die gelegentlich schwere cochleare Schwerhörigkeit, die sofort einer Stapedektomie folgt F erklärt jedoch nicht die verspätete Schwerhörigkeit, die einem ursprünglich guten Resultat folgt.

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No	LOCALIZATION	CLINICAL STAGE	HISTOLOGICAL TYPE
1	E PLICA PHARYNGOEPIGLOT	$T\ N_0$	B C. CA
2	E. PLICA ARYEPIGLOT V	$T\ N_1$	SQ. CA.
3	FALSE AND TRUE RIGHT VOCAL CORD INVASION OF THE THYRO HYO-EPIGL. REGION	$T\ N_0$	SQ. CA
4	VESTIBULAR	$T_4\ N_0$	SQ CA
5	ANTERIOR V PRE-EPIGLOTT. REGION	$T_3\ N_0$	B.C. CA
6	GLOTTIC AND UNDER-GLOT. EXTENDED TO VENTRICLE	$T\ N_0$	SQ CA.
7	GLOSSO LARYNGEAL	$T_4\ N_0$	SQ CA.
8	GLOTTIC	$T\ N_0$	SQ. CA
9	V	$T_4\ N_0$	SQ. CA.
10	V	$T\ N_3$	SQ. CA
11	M.	$T\ N_1$	SQ CA.
12	V	$T\ N_1$	BC. CA
13	M PLICA ARYEPIGLOT	$T_2\ N_0$	SQ CA
14	V. GLOTTIC AND UNDER-GLOT 1st TRACHEAL RING	$T\ N_0$	SQ. CA.
15	M PRE-EPIGLOT REGION	$T\ N_0$	SQ CA.
16	V	$T\ N_0$	SQ CA.
17	V SINUS PIRIFORMIS PLICA PHARINGO EPIGLOT	$T_4\ N_2$	SQ CA.
18	M.	$T\ N_0$	BC. CA.
19	V. WITH TUNNEL IN THYRO HYO EPIGL. REGION	$T_4\ N_0$	SQ. CA.
20	DEEP VENTRICULAR	$T\ N_0$	SQ. CA
21	V	$T_4\ N_3$	SQ CA
22	BASE OF THE TONGUE VALLECULE V	$T\ N$	SQ CA.
23	V WITH TUNNEL IN PRE-EPIGLOT SPACE	$T_4\ N_1$	SQ. CA
24	V.	$T_4\ N$	SQ. CA.
25	V THYRO-HYO-EPIGLOT. REGION BASE OF THE TONGUE	$T_4\ N_3$	SQ CA.
26	ANT. V ANT GLOTTIS PLICA GLOSSO EPIGLOTTIDEAN BASE OF THE TONGUE	$T_4\ N_3$	SQ CA.
27	V VENTRICLE VOCAL CORD THYRO-HYO EPIGLOT. REGION	$T_4\ N_1$	SQ. CA.
28	GLOSSO LARYNGEAL	$T\ N_1$	INDIFFERENTIA. CA.
29	V-RELAPSE TO HORIZONTAL UNDER-GLOTTIC LARYNGECTOMY	$T_4\ N_0$	SQ CA.
30	VENTRICLE FALSE CORD V ARYEPIGLOT AND PHARINGOEPIGL. PLICA	$T\ N$	INDIFFERENTIA. CA.
31	V PLICA GLOSSOEPIGLOTTIDEAN	$T_3\ N_0$	SQ. CA
32	M. ARYTENOID E	$T_3\ N_0$	SQ CA
33	V-ARYTENOID PLICA ARYEPIGLOT	$T_4\ N_2$	INDIFFERENTIA. CA.

V VESTIBULAR
E. EPIGLOTTIS
M. MARGINALIS

SQ CA SQUAMOUS CA
BC CA BASAL CELLS CA

Section 1

rotic phenomena if the tumour was not ulcerated or infected it should however be noted that such doses are most unlikely to heal a tumour which responded insufficiently to the customary doses of 7500–8500 r

These are the cases necessitating surgical completion to avoid administering doses over 8500 r

In the conditions for treatment outlined in paragraphs (I) (II) and (III) surgery appears indicated in the following circumstances

(1) In ascertaining the persistence of a tumour (which originally had logically been considered within control by radiotherapy alone) after 8–10 weeks from completion of radiotherapy

(2) On detecting relapses. With the above doses, relapses usually appear between the 8th and the 18th month from completion of treatment.

(3) With grave necroti phen mena over infected tumours, which give rise t seri us incidents f chondriti and perichondritis beyo d medical control (tibiotics, vitamins, cysteamine preparations, reparative cicatrizing preparations, horm nal restorers of th stromatic tissue)

After irradiation treatment, when partial surgery is performed uncovering the perichondral plane, the osteo-cartilaginous system of the laryngeal shield loses its apparent resistance to irradiation damage Nec rotic phenomena will then occur with considerable frequency also at a precocious stage If not corrected by prompt total laryngectomy such phenomena are hardly controllable and may lead to gradual tissue devasta tion likely to affect also the large vessels.

Section 1 shows, for each case the tumour location, the stage according to the TNM classification and the histological finding The stage break down is

T 1 nil T 2 3 cases T 3 11 cases T 4 10 cases

Biopsy was performed on all the 33 cases considered and gave the follow ing results

Spinocellular carcinomas 26 cases basocellular carcinomas 4 cases indifferentiated carcinomas 3 cases.

Section 2 gives, for each case the dose administered in function of time, the months of survival from beginning of treatment, the time lapsed from completion of radiotherapy to surgery

Mention was made earlier of the doses applied for irradiation of the larynx through a single anterior field with electron beams, of the pref erable dose fractionation and of the post-irradiation damage

The time span, between completion of radiotherapy and start of surgery of the cases under consideration, ranges from 10 days to 12 months Quite differently from what is observable after conventional Roentgen therapy and after cobalt therapy such wi lely different time spans did not evidence significant differences in operational haemorrhage and in wound cicatriza tion However the time span suggested between completion of radiotherapy and commencement of urgery is 2–3 months, enough to disperse the ac tion f radiotherapy Possible tissue damage arising during such time is always moderate and causes no increase in difficulty of operation

Section 3 di plays, for each case, the type of surgery performed, the presence or absence of neopla tic residues histologically ascertained on

Nº	LOCALIZATION	CLINICAL STAGE	HISTOLOGICAL TYPE
1	E PLICA PHARYNGOEPIGLOT	$T\ N_0$	B C. CA.
2	E. PLICA ARYEPIGLOT V	$T\ N_1$	SQ. CA.
3	FALSE AND TRUE RIGHT VOCAL CORD INVASION OF THE THYRO HYO-EPIGL REGION	$T\ N_0$	SQ. CA.
4	VESTIBULAR	$T_4\ N_1$	SQ CA.
5	ANTERIOR V PRE-EPIGLOTT REGION	$T_3\ N_0$	B.C. CA
6	GLOTTIC AND UNDER GLOT. EXTENDED TO VENTRICLE	$T\ N_0$	SQ. CA.
7	GLOSSO LARYNGEAL	$T_4\ N_3$	SQ. CA
8	GLOTTIC	$T\ N_0$	SQ CA.
9	V	$T_4\ N_0$	SQ CA.
10	V	$T\ N_3$	SQ CA
11	M	$T\ N_1$	SQ. CA.
12	V	$T\ N_1$	BC CA.
13	M PLICA ARYEPIGLOT	$T\ N_3$	SQ CA
14	V GLOTTIC AND UNDER-GLOT 1st TRACHEAL RING	$T_3\ N_3$	SQ. CA
15	M. PRE-EPIGLOT REGION	$T_3\ N_0$	SQ. CA
16	V	$T\ N_0$	SQ CA.
17	V SINUS PIRIFORMIS PLICA PHARINGO EPIGLOT	$T_4\ N_2$	SQ CA
18	M.	$T\ N_0$	BC. CA.
19	V. WITH TUNNEL IN THYRO HYO EPIGL. REGION	$T_4\ N_0$	SQ. CA
20	DEEP VENTRICULAR	$T\ N_0$	SQ. CA.
21	V	$T_4\ N_2$	SQ CA
22	BASE OF THE TONGUE VALLECULE V	$T_3\ N_0$	SQ CA.
23	V WITH TUNNEL IN PRE-EPIGLOT SPACE	$T_4\ N_1$	SQ. CA.
24	V	$T_4\ N$	SQ. CA.
25	V. THYRO-HYO-EPIGLOT. REGION BASE OF THE TONGUE	$T_4\ N_3$	SQ. CA
26	ANT. V ANT GLOTTIS PLICA GLOSSO EPIGLOTTIDEAN BASE OF THE TONGUE	$T_4\ N_0$	SQ. CA.
27	V VENTRICLE VOCAL CORD THYRO-HYO EPIGLOT REGION	$T_4\ N_1$	SQ CA
28	GLOSSO LARYNGEAL	$T\ N_0$	INDIFFERENTIA. CA.
29	V-RELAPSE TO HORIZONTAL UNDER-GLOTTIC LARYNGECTOMY	$T_4\ N_2$	SQ CA
30	VENTRICLE FALSE CORD V ARYEPIGLOT. AND PHARINGOEPIGL. PLICA	$T\ N_2$	INDIFFERENTIA. CA.
31	V-PLICA GLOSSOEPIGLOTTIDEAN	$T_4\ N_0$	SQ CA.
32	M ARYTENOID E	$T\ N_1$	SQ CA.
33	V ARYTENOID PLICA ARYEPIGLOT	$T\ N_2$	INDIFFERENTIA CA.

V VESTIBULAR
E. EPIGLOTTIS
M. MARGINALIS

SQ CA. SQUAMOUS CA
B.C.CA. BASAL CELLS CA

Section 1

rotic phenomena if the tumour was not ulcerated or infected it should however be noted that such doses are most unlikely to heal a tumour which responded insufficiently to the customary doses of 7500–8500 r

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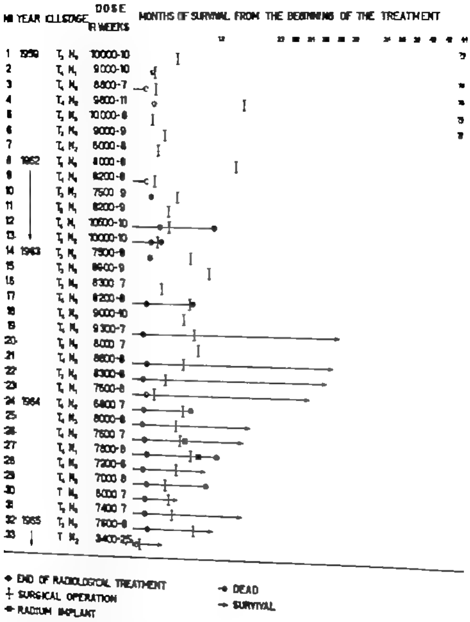
In the conditions for treatment outlined in paragraphs (I) (II) and (III) surgery appears indicated in the following circumstances



Section 2

The f llowing wa however observed

The process of tissue reparation failed in on case with which the following radiotherapy had been employed (a) 8200 r with electrons over 76 days on the lary x, (b) 3750 with telecobalt therapy o er 31 days and 2000 r with elec tron in 11 day on the cervical chains. 28 days after surgery the patient deceased due t carotid haemorrhage brought on by necrosis.

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seriated sections of the piece operated the performance of the irradiated tissues during and after surgery the causes of the 11 deceases

Section 1

Operational techniques adopted

	Cases
Total laryngectomy	[illegible]
Total laryngectomy + neck monolateral dissection	15
Total laryngectomy + neck bilateral dissection	[illegible]
Total laryngectomy + partial tracheotomy	1
Total laryngectomy + partial thyroidectomy	2
Total laryngectomy + subglossectomy	4
Total laryngectomy + subglossectomy + neck monolateral dissection	[illegible]
Total laryngectomy + subglossectomy + neck bilateral dissection	1
Transverse supraglottic laryngectomy	2
Transverse supraglottic laryngectomy + neck monolateral dissection	2

Section 2

Presence of tumour residues in the piece operated by stage

Stag	Cases	Tumour residues Yes	No
T 2	3	1	2
T 3	11	6	5
T 4	10	12	7

Section 3

Performance of irradiated tissues during and after surgery

(a) With *total laryngectomy* the results were mostly favourable

The cutis is easily incisible suture cohesion and cicatrization are normal and obtained also thanks to particular methods aimed at keeping the edges well nourished such as adopting "Z plastic surgery on the neck cutis (*following the techniques indicated by* Aubry Jos and Chouard) ensuring continuous suction of blood and serum from the zone of operation by means of Redon apparatus, and using a *compressive but resilient* dressing Tissue haemorrhage is not beyond normal therefore the usual employment of hypotension is unnecessary the muscles never caused concern In four cases, necrosis *of one or both of the* laminae of the thyroid cartilage though serious, did not prejudice the correct restoration of the cutis and mucoses after surgery

In two cases there appeared a spontaneous pharyngostoma, very limited and caused by precocious necrosis f the tissues.

(b) With *hori-ontal supragl ttic laryngect my* the situation is most different. It i f it that the unf vourable experience in similar cases could be explained by the fact that the irradiated cartilage, though histologically normal, undergoes such biological modification a to become an easy prey of ambient bacterical flora. Obviously this problem does not arise with total laryngectomy surgery which inv lves the removal of all of the osteocartilaginous mass. *Of the 4 cases* operated f r transverse supraglottic only one recovered without in idents a sec ond case developed necrosis, required total laryngectomy and is survi ing without any traces of tumour a third case died after months with post operational necrosi f llowed by bronchopneumonia a fourth case died after 8 day with cardio-circulat ry collapse

(c) Post perational rad therapy In two cases the treatment had provided irradiation plus surgery consisting of radiotherapy with electrons and sub-sequent surgical intervention. Such composite treatment was subsequently com pleted by implant of radium needles in the tongue base through the pharyngo-stoma 30 and 2o d y after surgery on the respective cases, since histological invest gation had revealed the survival of neoplastic ti sue islands in the above zone Of the two cases, one died with a relapse 15 months after the beginning f treatment the other is surviving after 16 months without manifest signs of eoplasia.

Of the 33 patients treated with irradiation plus surgery from 1959 to June 1965 21 are surviving Of the latter 2 belonged to stage II 9 to stage III and 10 to stage IV

The following are the causes for the decease of 12 patients

Tumour relapse	1
Visceral metasta is	4
Post-operational haemorrhage and local necrosis	2
Causes other than neoplastic	3

CONCLUSION

It should be premised that, of a total of about 250 cases of laryngeal and hypopharingeal tumours treated with irradiation with high-energy lectron beams of the Betatron from early 1959 to June 1965 only in 33 cases resort was made to complementary surgery This will witness th high percentage of success obtained by us by electron radiotherapy lone

From our experience it emerged that the employment of electrons through a singl direct, anterior or anterio-lateral field with a erage doses of 7400 8500 r over 8–9 weeks, *allows* a more technically correct treatment f th neopla tic f cus a compared to con entional radiotherapy—with no prejudice t the pos ibility of surgery which might be required after radiotherapy Operation on the irradiated zone *in fact*, never caused par ticular difficulties to the urgeon, wherea cicatrization was mostly normal

N°	STAGE	TYPE OF SURGICAL OPERATION	HISTOLOGICAL TUMOUR REST AFTER RADIOTH	IMMED. HEALING AFTER OPERAT. SKIN	IMMED. HEALING AFTER OPERAT. MUCOSA	LATE HEALING AFTER OPERAT.	NECROSIS	DEAD relapse	DEAD distant metastases	DEAD other causes	DEAD haemorrh. after operat.
1	T_3N_0	T.L. – N.D.			+ + +	+	–				
2	T N	T.L. N.D.	+	+	+	+ +				●	
3	T_4N_0	T.L. – N.D.		+	+ + +	+					
4	T_4N_2	T.L. – N.D.	–		+ +	+					
5	T_3N_0	T.L. – N.D.	+	+	+ + +	+					
6	T_3N_0	T.L. – N.D.				+	–				
7	T_4N_0	T.L. PARTIAL GLOSSOTOMY BILAT. N.D.	+	– +	+ + +	+ +	–		●		
8	T_3N_0	T.L. N.D.	RELAPSE	+ +	+	+ + +	–				
9	T N_0	T.L. N.D.		+ +	+ + +	+	a		●		
10	T_3N_3	T.S.L.		+ + +	+ + +	+ +	+		●		
11	T_2N_1	T.L. N.D.	–	+	+ + +	+	–				
12	T_4N_1	T.S.L.	–	– –	–	– –	+			●	
13	T N_1	T.S.L. N.D.		+	+					●	
14	T_3N_0	T.L.-3 RINGS OF TRACHEA THYROID LOBE				+ +					
15	T_3N_0	T.L. BILATERAL N.D.	+	–		+ +	–				
16	T_3N_0	T.L.	+		+	+ +	–				
17	T_4N_2	T.L. – N.D.			+		–		●		
18	T N_0	T.L. PARTIAL GLOSSOTOMY		– –		+	+			●	
19	T N_0	T.L. N.D. PARTIAL GLOSSOTOMY	–	– –	–	– –	b				
20	T_3N_0	T.L. 3 RINGS OF TRACHEA	–	– –		–				●	
21	T_4 N	T.S.L. T.L. AFTER 1 MONTH		+ +	+ + +	+ +	+				
22	T_3N_0	T.L. N.D.	–	+	+	+ + +					
23	T N_1	T.L. – N.D.	–	+ + +	+ +	+ + +	–				
24	T_4N_3	T.L. N.D.-CAROTIC RES.-R. THYROID CON.	–	– –	– – –	–	c				●
25	T_4N_3	T.L. PART. GLOSSOTOMY PHARINGOSTOMA	+	+ +	+ + +		–				
26	T N_0	T.L. PART. GLOSSOTOMY PHARINGOSTOMA	+	+ +	+ +		–				
27	T_4N_1	T.L.	–	+ + +	+	+ +	–	●			
28	T N_0	T.L. PARTIAL GLOSSOTOMY		–	–	– –					
29	T_4N_3	T.L. – N.D.		+ +	+ +		d				●
30	T_4N_3	T.L. N.D.		+ + +	+ +	+ +					
31	T_4N_0	T.L. N.D.-PARTIAL GLOSSOTOMY	+	–	– –	–	+				
32	T_3N_0	T.L. – N.D.	+		+ + +	+ + +	–				
33	T_4N_2	T.L.-BILATERAL N.D.	+	+	+ + +	+ + +	–				

T.L. – TOTAL LARYNGECTOMY
N.D. – NECK DISSECTION
T.S.L. – TRANVERSE SUPRAGLOTTIC LARYNGECTOMY

a BASE OF THE TONGUE, AFTER 4 MONTHS
b SPONTANEOUS PHARYNGOSTOMA
c NECR. IMMEDIATE
d SKIN NECR. AFTER 6 MONTHS

Section 3

In two cases (respectively one of total laryngectomy with subgl ssectomy and the other of total laryngectomy performed following supraglottic horizontal laryngectomy) limited necrosis of the tissues (cutis and mucosa) settling in 1 and 2 months respectively from intervention of surgery in each case did not prevent the subsequent normal cicatrization of the surgical incision.

In one case retarded (after 4 months) necrosis of the tongue has caused a grave haemorrhage which was controlled by ligating the carotid.

In two cases there appeared spontaneous pharyngostoma, very limited and caused by precocious necrosis of the tissues.

(*b*) With *horizontal supraglottic laryngectomy* the situation is most different. It is felt that the unfavourable experience in similar cases could be explained by the fact that the irradiated cartilage, though histologically normal, undergoes such biological modification as to become an easy prey of ambient bacterial flora. Obviously this problem does not arise with total laryngectomy surgery which involves the removal of all of the osteocartilaginous mass. Of the 4 cases operated for transverse supraglottic only one recovered without incidents; a second case developed necrosis, required total laryngectomy and is surviving without any traces of tumour; a third case died after 5 months with post-operational necrosis followed by bronchopneumonia; a fourth case died after 8 days with cardio-circulatory collapse.

(*c*) *Post-operational radiotherapy*. In two cases the treatment had provided irradiation plus surgery, consisting of radiotherapy with electrons and subsequent surgical intervention. Such composite treatment was subsequently completed by implant of radium needles in the tongue base through the pharyngostoma, 30 and 25 days after surgery on the respective cases, since histological investigation had revealed the survival of neoplastic tissue *islands in the above zone*. Of the two cases, one died with a relapse 1 month after the beginning of treatment; the other is surviving after 16 months without manifest *signs of* neoplasia.

Of the 33 patients treated with irradiation plus surgery from 1959 to June 1963, 21 are surviving. Of the latter 2 belonged to stage II, 9 to stage III and 10 to stage IV.

The following are the causes for the decease of 12 patients:

Tumour relapse	1
Visceral metastasis	4
Post-operational haemorrhage and local necrosis	2
Causes other than neoplastic	5

CONCLUSION

It should be premised that of a total of about 250 cases of laryngeal and hypopharingeal tumours treated with irradiation with high-energy electron beams of the Betatron from early 1959 to June 1963, only in 33 cases resort was made to complementary surgery. This will witness the high percentage of success obtained by us by electron radiotherapy alone.

From our experience it emerged that the employment of electrons through a single direct, anterior or anterio-lateral field with average doses of 7500–8500 r over 8–9 weeks, allows a more technically correct treatment of the neoplastic focus as compared to conventional radiotherapy—with no prejudice to the possibility of surgery which might be required after radiotherapy. Operation on the irradiated zone, in fact, never caused particular difficulties to the surgeon, whereas cicatrization was mostly normal.

The treatment combining radiotherapy and surgery was applied in the following cases

1 widespread tumours of the larynx and hypopharynx involving the valleculae the tongue base and the pharyngo-epiglottic plicae
2 endolaryngeal tumours incompletely sterilized by radiotherapy
3 widespread tumours of the anterior vestibule with which preliminary electron therapy had been aimed at reducing the neoplasia within the limits for a correct partial supraglottic surgery after radiotherapy
4 tumour relapses after completion of radiotherapy
5 ulcerated and infected tumours, where radiotherapy had induced serious necrosis, chondritis, perichondritis beyond control by medical treatment
6 cases in which a previous partial operation following radiotherapy had induced necrotic phenomena of the laryngeal cartilaginous system in such circumstances timely total laryngectomy was able to correct a condition of serious distress of the osteo-cartilaginous tissues which apparently resist irradiation until surgical intervention or inflammatory processes uncover the perichondral plane

The 33 cases subjected to irradiation plus surgery belonged chiefly to widespread tumour affections classified in the third and mostly in the fourth stage the survivals broken down by stage are 2 out of 3 in stage T 2 9 out of 11 in stage T 3 and 10 out of 19 in stage T 4 A remarkable point is the survival of a few T 3 and T 4 cases over 6 years after the beginning of treatment

Our results with a correct treatment with combined irradiation and surgery in a number of cases—which though comparatively moderate represent the most extensive statistics published to date—are quite gratifying chiefly if we consider the spread of the neoplastic affections

It can thus be stated that in cases where complete success cannot be achieved by radiotherapy with high-energy electrons of the Betatron—in our experience to be considered today as the therapy most indicated for laryngeal and hypopharyngeal tumours, excluding ventricular affections—the combination of radiotherapy and surgery will allow satisfactory results also with remarkably widespread neoplastic affections.

RESUME

Les auteurs ont analysé leurs résultats sur 33 cas de tumeurs du larynx et de l hypopharynx obtenus avec combinaison radiochirurgicale Le traitement radiologique préopératoire a été réalisé par les électrons d'haute énergie d un Bétatron (14–3 MeV) en donnant des doses de 7000–10 000 r en 7–10 semaines sur un champ unique antérieur ou antéro-latéral L intervention a été réalisée en cas de tumeurs particulièrement étendus (dont le but du traitement préopératoire était de réduire la néoplasie aux limites d opérabilité) dans les cas de tumeurs incomplètement stérilisés par les électrons, en cas de récidive lorsque une grave

nécrose n était pas dominée par le traitement médical. L'intervention n a jamais présenté des difficultés la cicatrisation a été toujours satisfaisante Les auteurs décri ent leurs résultats pour des cas suivis jusqu à cinq ans les résultats doi- ent être considérés très favorables quand on regard l'extension considérable d la plus part des néoplasies traitées.

ZUSAMMENFASSUNG

Die Autoren beschreiben ihre Ergebnisse über 33 Fäll von Kehlkopf und Hypopharynx-Geschwülsten die nach der Behandlu g mit schnellen Elektronen (14 [illegible] MeV) operiert wurden. Dosen von rund 7000 bis 10 000 r in 7–10 Wochen durch ein einzelnes direktes vorderes Feld wurden angewandt. Ein operativer Eingriff wurde durchgeführt bei besonders ausgedehnten Geschwülsten (wo die Radiotherapie den Zweck hatte, die Operation zu ermöglichen) [illegible] Fällen w die Radiotherapie die Geschwülst nicht völlig sterilisiert hatte in residivierten Fallen in Fällen von schwerer Nekrose die eine ärztliche Therapie nicht beherrschen konnte Keine Schwierigkeiten wurden beobachtet bei dem operati en Eingriff die Vernarbung war immer befriedigend Die positiven Ergebnisse die sich für einige Fälle auf eine Zeitspanne von über 5 Jahren beziehen sind sehr günstig, auch in Anbetracht der Ausdehnung der meisten behandelten Geschwülste

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The treatment combining radiotherapy and surgery was applied in the following cases:

1. widespread tumours of the larynx and hypopharynx involving the valleculae, the tongue base and the pharyngo-epiglottic plicae;
2. endolaryngeal tumours incompletely sterilized by radiotherapy;
3. widespread tumours of the anterior vestibule, with which preliminary electron therapy had been aimed at reducing the neoplasia within the limits for a correct partial supraglottic surgery after radiotherapy;
4. tumour relapses after completion of radiotherapy;
5. ulcerated and infected tumours, where radiotherapy had induced serious necrosis, chondritis, perichondritis beyond control by medical treatment;
6. cases in which a previous partial operation following radiotherapy had induced necrotic phenomena of the laryngeal cartilaginous system. In such circumstances, timely total laryngectomy was able to correct a condition of serious distress of the oteo-cartilaginous tissues which apparently resist irradiation until surgical intervention or inflammatory processes uncover the perichondral plane.

The 33 cases subjected to irradiation plus surgery belonged chiefly to widespread tumour affections classified in the third and mostly in the fourth stage; the survivals broken down by stage are: 2 out of 3 in stage T 2, 9 out of 11 in stage T 3 and 10 out of 19 in stage T 4. A remarkable point is the survival of a few T 3 and T 4 cases over 6 years after the beginning of treatment.

Our results with a correct treatment with combined irradiation and surgery in a number of cases—which, though comparatively moderate, represent the most extensive statistics published to date—are quite gratifying, chiefly if we consider the spread of the neoplastic affections.

It can thus be stated that in cases where complete success cannot be achieved by radiotherapy with high-energy electrons of the Betatron—in our experience to be considered today as the therapy most indicated for laryngeal and hypopharyngeal tumours, excluding ventricular affections—the combination of radiotherapy and surgery will allow satisfactory results also with remarkably widespread neoplastic affections.

RESUME

Les auteurs ont analysé leurs résultats sur 33 cas de tumeurs du larynx et de l'hypopharynx obtenus avec combinaison radiochirurgicale. Le traitement radiologique préopératoire a été réalisé par les électrons d'haute énergie d'un Bétatron (14–32 MeV) en donnant des doses de 7000–10 000 r en 7–10 semaines sur un champ unique antérieur ou antéro-latéral. L'intervention a été réalisée en cas de tumeurs particulièrement étendus (dont le but du traitement préopératoire était de réduire la néoplasie aux limites d'opérabilité), dans les cas de tumeurs incomplètement stérilisés par les électrons, en cas de récidive, lorsque une grave

dix jours avant le début du travail, y étaient conservés jusqu'à la fin. L'éclairage était celui du laboratoire.

L'appareil utilisé pour stimuler les canaux semi-circulaires horizontaux a déjà été décrit par l'un de nous (Gribenski, 1964). Quelques précisions nouvelles doivent être données ici. Le moteur à courant continu qui entraîne le plateau est alimenté par une pile de façon à avoir une tension stable et une vitesse uniforme. La pile, de 90 volts, est formée de 60 éléments de 1,5 volt montés en série; on peut ainsi donner à la tension toutes les valeurs, de 1,5 V en 1,5 V, entre 0 et 90 volts; un potentiomètre permet d'obtenir les valeurs intermédiaires. L'arrêt de la rotation s'effectue brusquement mais sans choc, grâce à l'emploi, d'une part, de deux plateaux superposés, le plateau inférieur étant fixé sur l'arbre du moteur et le plateau supérieur tournant librement autour de son axe; d'autre part, d'un frein à patin de caoutchouc qui peut appuyer sur le bord du plateau supérieur et dont le déplacement coupe le circuit d'alimentation du moteur.

L'animal est soumis à une rotation à vitesse uniforme pendant un temps suffisamment long (une minute environ) pour que l'appareil vestibulaire, stimulé au démarrage de la rotation, soit revenu au repos. L'arrêt de la rotation, effectuant en une fraction de seconde, de la même façon à toutes les vitesses de rotation utilisées, il y a proportionnalité entre la décélération et la vitesse à laquelle tournait le plateau avant l'arrêt. Cette proportionnalité nous autorise à indiquer les valeurs de stimulation sous la forme de vitesses de rotation, bien que le stimulus adéquat du canal semi-circulaire soit l'accélération angulaire. Le seuil de stimulation postrotatoire est alors exprimé par la vitesse de rotation qui permet d'obtenir à l'arrêt, dans 50 p. 100 des cas, une réaction juste perceptible (léger mouvement de la tête dans le sens de la rotation).

Les seuils de stimulation ont été déterminés méthodiquement comme le montre le tableau 1, qui correspond à une grenouille encore pourvue de la vue (grenouille n° 4). Nous avons recherché la valeur des seuils de stimulation pour les deux sens de rotation, horaire et antihoraire, par les méthodes ascendante et descendante, au cours de 5 journées quelconques. Si l'on examine par exemple les réponses de la grenouille n° 4 pour une rotation de sens horaire pendant la journée du 21 janvier, on remarque les résultats suivants: à une vitesse de 7,0 °/s., la grenouille, ayant subi 10 fois la même stimulation à quelques minutes d'intervalle, a réagi 10 fois à l'arrêt d'une rotation; à la vitesse de 6,7 °/s., elle réagit encore 10 fois sur 10; ensuite la fréquence des réactions diminue en même temps que décroît la vitesse de rotation. La grenouille ne réagit plus que 5 fois sur 10 avec une vitesse de 4,9 °/s. et 1 fois sur 10 à 4,7 °/s. Conformément à la règle habituelle, nous avons pris pour valeur du seuil la vitesse à laquelle la grenouille réagit 5 fois sur 10, soit, dans ce cas précis, 4,9 °/s. Les mêmes mesures ont été faites par la méthode ascendante (c'est-à-dire dans le sens des stimulations d'intensité croissante) et les résultats montrent que, pour une rotation de sens horaire, le même jour, le seuil a la valeur de

INFLUENCE DE LA VISION SUR LE SEUIL DES RÉACTIONS VESTIBULAIRES POSTROTATOIRES

Réactions dues à la stimulation des canaux semi-circulaires horizontaux

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On étudie chez la Grenouille, l'influence de la vision sur le seuil des réactions vestibulaires postrotatoires (réactions dues à la stimulation des canaux semi-circulaires horizontaux). La stimulation est produite par l'arrêt d'une rotation uniforme, *arrêt réalisé en un temps très court*, ce qui permet d'exprimer la valeur de la stimulation sous la forme d'une vitesse de rotation. Les expériences portent sur des grenouilles d'abord pourvues de la vue, ensuite rendues aveugles par section des nerfs optiques. Pour chacune d'elles, le seuil — la plus petite vitesse de rotation capable de produire à l'arrêt une réaction juste perceptible (léger mouvement de la tête dans le sens de la rotation) — est plus élevé lorsque l'animal voit que lorsqu'il est aveugle. Il apparaît donc que la vision tend à inhiber les réactions vestibulaires postrotatoires.

INTRODUCTION

Des expériences faites par Mowrer (1937) chez l'homme montrent que *la présence de la vue pendant une rotation dans le plan horizontal* diminue la durée du nystagmus postrotatoire. La même remarque a été faite pour les réactions postrotatoires du Pigeon (Mowrer, 1935) et du Vairon (Loewenstein, 1932); elle a sans doute une valeur générale. On peut donc penser que le seuil de stimulation postrotatoire (valeur de la stimulation la plus faible qui produise une réaction juste perceptible à l'arrêt de la rotation) sera plus élevé chez un animal qui voit que chez le même animal rendu aveugle. Cependant aucun travail n'a été fait jusqu'à présent sur ce sujet et, afin de vérifier cette hypothèse, nous avons, chez la Grenouille, comparé les seuils de stimulation pour les réactions postrotatoires lorsque la vision était possible et lorsqu'elle était supprimée (les animaux étant rendus aveugles par section des nerfs optiques).

EXPÉRIENCES ET RÉSULTATS

Les expériences ont porté sur [illegible] grenouilles (*Rana esculenta* L.). Les animaux, placés à la température du laboratoire (22 à 25 C) au moins

dix jours avant le début du travail, y étaient conservés jusqu'à la fin. L'éclairage était celui du laboratoire.

L'appareil utilisé pour stimuler les canaux semi-circulaires horizontaux a déjà été décrit par l'un de nous (Gribenski, 1964). Quelques précisions nouvelles doivent être données ici. Le moteur à courant continu qui entraine le plateau est alimenté par une pile de façon à avoir une tension stable et une vitesse uniforme: la pile, de 90 volts, est formée de 60 éléments de 1,5 volt, montés en série; on peut ainsi donner à la tension toutes les valeurs, de 1,5 V en 1,5 V, entre 0 et 90 volts; un potentiomètre permet d'obtenir les valeurs intermédiaires. L'arrêt de la rotation s'effectue brusquement, mais sans choc, grâce à l'emploi, d'une part, de deux plateaux superposés, le plateau inférieur étant fixé sur l'arbre du moteur et le plateau supérieur tournant librement autour de son axe; d'autre part, d'un frein à patin de caoutchouc qui peut appuyer sur le bord du plateau supérieur et dont le déplacement coupe le circuit d'alimentation du moteur.

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TABLEAU 1 *Grenouille n° 4 avant section des nerfs optiques*

(Chacun des signes indique le résultat d'un essai; + : présence d'une réaction; − : absence de réaction)

21 janvier

Rotation le sens horaire		Rotation de sens antihoraire	
7,9 ++++++++++	4,7 −−+−−−−−−−	6,2 +++−++++++	4,5 +−+−−−−−−−
6,7 ++++++++++	5,1 +−+−+−+−−+	5,8 ++−−++−+++	5 −−+−−++−+−
6,4 +++++−++++	5,3 ++++++++−+	5,6 ++++−++−+−	5,5 −+++++++−+
6 ++−++++−++	5,7 ++++++++++	5,2 +−+−−−−+++	5,8 +++++++−+−
5 ++−−++++++		5 −++−−−−−−+	6,3 ++++++++++
5,3 ++−+−++−++		4,5 +−+−−−−−−−	
4,9 +−−−−++++−			
4,7 −−+−−−−−−−			
seuil 4,9	seuil 5,1	seuil 5,2	seuil 5,2

Seuil journalier 5 — Seuil journalier 5,2

25 janvier

Rotation le sens horaire		Rotation de sens antihoraire	
6,3 ++++++++++	4 −−−−−−−−−−	6,3 +++++ ++−+	4 −−−−−−−−−−
5,6 ++−+−−++++	4,6 −−−−−−−−−+	5,8 +−−+−+++−+	4,8 −+−−−+++−−
5,2 +−−+−++−−+−	4,9 −−−−−−−−++	5,1 ++++−+−+−+−	5 −+−−+++−++−
4,9 ++−+−−−−++−	5,1 −−+−−+−++−	5,2 −++−−−−++−	5,7 +++−++++++
4,6 −−+−+−−−−−	5,5 −+−++−++++	4,5 −+−−−−+−−−	
4 −−−−−−−−−−	6 +−+++−−+++	4 −−−−−−−−−−	
	6,3 ++++++++++		
seuil 4,9	seuil 5,3	seuil 5,3	seuil 5

Seuil journalier 5,1 — Seuil journalier 5,1

26 janvier

Rotation le sens horaire		Rotation de sens antihoraire	
6,8 ++++++++++	4,1 −−+−+−−−−−	7,1 ++++++++++	4,3 −−−−−+−−+−
6,1 +−++− −+++	4,5 −−−−−−−−+−	6 ++++−+−+−−	4,8 −++−− +−−
5,6 ++−+++−++−	4,9 +−−+−+−−−−−	5,5 +−+−−+++ +	5,2 +− +−++−−+
5 +−−−++−+−+−	5,3 + −−+−+++−	5 −++−−+−+−+	6 +++++++++
4,5 +−+−−−−−−+−	5,9 ++−+−++−+−	4,5 −−+−+−+−−−	
4,1 −−+−+−−−−−	6,5 −+ +− ++ −	4,3 −−−−−−+−−+−	
	7,3 +++++ + +		
seuil 5	seuil 5,1	seuil 5	seuil 5

Seuil journalier 5,1 — Seuil journalier 5

27 janvier

Rotation le sens horaire		Rotation de sens antihoraire	
6,9 ++++++++++	4,9 −−−− −−−−−	6,8 ++++++++++	4,6 − −−−−−−−
6,2 ++++++++++	5,3 −−+− − −−−	6 + ++++	5 −−− −−− −
5,7 ++++−+ +−−+	5,5 +−− −−+	5,3 + ++− − −	5,5 − −−+
5,3 −−−−+−−−+−	5,9 +++++−−+	5,1 −+−− −− −	5,7 − − +
4,9 −−−−+−−−−−	6,3 +++++++++−	4,6 +− −−−−−−−	6,1 + −+
seuil 5,5	seuil 5,1	seuil 5,2	seuil 5,2

Seuil journalier 5,1 — Seuil journalier 5,2

[illegible] janvier

Rotation le sens horaire		Rotation de sens antihoraire	
7 ++++ + ++	4,2 −−−− −− −	6,5 ++ + + +	4,2 − −−
6,2 ++++ + ++	4,4 −−+−−−−−−−	5,9 −++ +	4,5 − −
5,7 ++++ − +−	4,7 −−+−−+−−−	5,4 −+−+−+ +	4,9
5,3 −−+ + − +	5 −−+−−+−−	5 −−−− −	5,3
5 −+−−−++−−−	5,5 −− −+	4,6 −− −− − −−	5,9
4,5 −−+−−−−−− −	6,3 +++ ++ +	4,2 −−− −−−−−−	6,4
4,2 −−−−−−−−−			
seuil 5,1	seuil 5,3	seuil 5	seuil 5,3

Seuil journalier 5,2 — Seuil journalier 5,1

Seuil horaire (moyen): 5,2 — *Seuil antihoraire (moyen)* 5,1

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TABLEAU 2. *Valeur des seuils de stimulation postrotatoire (seuils moyens) chez des grenouilles normales et aveugles pour des rotations de sens horaire et antihoraire*

(La valeur des seuils est exprimée en degrés par seconde.) Les chiffres de 1 à 9 désignent les grenouilles.

	Rotation de sens horaire		Rotation de sens antihoraire	
	Grenouille normale	Grenouille aveugle	Grenouille normale	Grenouille aveugle
1	5,0	4,1	4,8	3,0
2	5,2	4,3	5,0	3,8
3	2,1	3,3	3,3	2,0
4	5,2	3,7	5,1	3,5
5	5,3	4,3	5,2	4,3
6	[illegible]	4,6	5,2	4,2
7	5,2	3,6	5,0	3,2
8	4,0	2,7	3,0	2,7
9	3,0	2,8	3,1	2,6

5,1 /s. La moyenne de ces 2 valeurs, soit 5 /s., représente le seuil de ce jour (ou seuil journalier) pour cette grenouille et pour une rotation de sens horaire.

La même série de mesures a été réalisée le même jour pour une rotation de sens antihoraire. Ces opérations ont été répétées au cours de 5 journées prises au hasard (pour cette grenouille, les 21, 25, 26, 2 et 29 janvier). La moyenne des valeurs des 5 seuils journaliers pour un sens de rotation donne le seuil moyen, soit, pour la grenouille n° 4, une valeur de 5,2 /s. pour une rotation de sens horaire et 5,1 /s. pour une rotation de sens antihoraire. Ainsi, la détermination du seuil moyen pour chaque sens de rotation est le résultat de 500 à 600 observations. Ces mesures ont été répétées sur la même grenouille après section des nerfs optiques.

Les seuils sont peu différents pour les deux sens de rotation : la sensibilité des canaux semi-circulaires horizontaux, dans ces conditions, est la même dans les deux sens.

Le tableau 2 indique les valeurs des seuils moyens (moyennes des valeurs de 5 seuils journaliers) des 9 grenouilles, d'abord lorsqu'elles voyaient, ensuite lorsqu'elles étaient privées de la vue. L'examen de ce tableau montre que le seuil déterminé pour une rotation de sens horaire ou de sens antihoraire chez une grenouille qui voit est supérieur au seuil déterminé pour le même sens de rotation, chez le même animal rendu aveugle. Il en est ainsi pour les animaux dont le seuil est le plus bas (ex. : n° 8 et 9) et pour ceux dont le seuil est relativement élevé (ex. : n° 4 et 5), c'est-à-dire pour des animaux dont la sensibilité à ce type de stimulation a une valeur très différente.

TABLEAU 1 *Grenouille n° 4 avant section des nerfs optiques*

(Chacun des signes indique le résultat d'un essai; + : présence d'une réaction; — : absence de réaction)

Rotation de sens horaire				Rotation de sens antihoraire			
21 janvier							
7,9	++++++++++	4,7	—+————————	6,2	+++—++++++	4,5	+—+———————
6,7	++++++++++	5,1	+—+—+—+——+	5,8	++——++—+++	5	——+——++—+—
6,4	+++++—++++	5,3	++++++++—+	5,6	++++—++—+—	5,5	—+++++++—
6	++—++++—++	5,7	++++++++++	5,2	+—+————+++	5,8	++++++—++—
5,7	++——++++++			5	—++——————+	6,3	++++++++++
5,3	++—+—++—++			4,5	+—+———————		
4,9	+————++++—						
4,7	——+———————						
seuil. 4,9		seuil. 5,1		seuil. 5,2		seuil. 5,2	
Seuil journalier 5				Seuil journalier 5,2			
25 janvier							
6,3	++++++++++	4	——————————	6,3	++++++++—+	4	——————————
5,0	++—+——++++	4,6	—————————+	5,8	+——+—+++—+	4,8	—+———+++——
5,2	+—+—++——+—	4,9	————————++	5,4	+++—+—+—+—	5	—+——++—++—
4,0	++—+————++—	5,1	——+——+—++—	5,2	—++———++——	5,7	+++—+++++
4,0	——+—+—————	5,5	—+—++—++++	4,5	—+————+———		
4	——————————	6	+—+++——+++	4	——————————		
		6,3	++++++++++				
seuil. 4,0		seuil. 5,3		seuil. 5,3		seuil. 5	
Seuil journalier 5,1				Seuil journalier 5,1			
26 janvier							
6,8	++++++++++	4,1	——+—+—————	7,1	++++++++++	4,3	—————+——+—
6,1	+—++—+—+++	4,5	————————+—	6	++++—+—+——	4,8	—++——++———
5,6	++—+++—++—	4,9	+——++—————	5,5	+—+——+++++	5,2	+—++—++——+
5	+———+++—+—	5,3	++——+—+++—	5	—++——+—+—+	6	++++++++++
4,5	+—+—————+—	5,9	+ —+—++—+—	4,5	——+—+—+———		
4,1	——+—+—————	6,5	—+ +—++++—	4,3	—————+——+—		
		7,3	++++++++++				
seuil. 5		seuil. 5,1		seuil 5		seuil 5	
Seuil journalier 5,1				Seuil journalier 5			
27 janvier							
6,6	++++++++++	4,9	———— —————	6,8	++++++++ ++	4,6	+—+———————
6,2	++++++++++	5,3	——+—+—+ ——	6	++++++ +++	5	———+———+ —
5,7	+++—+++——+	5,5	+——+——++ +	5,3	++++—+—+—	5,5	— + + ——
5,3	—————+———+—	5,9	++++——++ —	5,1	—+—— ——+—+	5,7	— — + ++
4,9	———— —————	6,3	+ +++ —	4,6	— ———————	6,1	—+
seuil 5,5		seuil. 5,1		seuil. 5,2		seuil. 5,2	
Seuil journalier 5,1				Seuil journalier 5,2			
[illegible] janvier							
7	++++ ++ ++	4,2	——————————	6,5	++ ++++	4,2	——— ——— ——
6,2	++++++++++	4,4	——+———————	5,9	—++ + + +	4,5	—— ——— ——
5,7	++++++— +—	4,7	——+——++———	5,1	—+—+—++ +	4,9	—— — ——
5,3	——++++— ++	5	—— ——+——++	5	—————+ — +	5,3	—— —— —
5	—+———++———	5,5	—— —++++++	4,6	—— —— — ——	5,9	— — + —
4,5	——+———————	6,3	++++++++++	4,2	———+——————	6,1	
4,2	——————————						
seuil. 5,1		seuil. 5,3		seuil 5		seuil 5,3	
Seuil journalier 5,2				Seuil journalier 5,1			

Seuil horaire (moyen): 5,2

Seuil antihoraire (moyen) 5,1

CONCLUSION

La vision chez la grenouille élève le seuil pour les réactions postrotatoires dues à la stimulation des canaux horizontaux. La présence de la vue pendant et après la rotation, inhibe donc partiellement les réactions postrotatoires. L'inhibition est plus ou moins marquée selon les individus, comme on peut le voir sur la figure : par exemple elle est importante pour la grenouille n° 7 (le groupe des croix et le groupe des points sont distants l'un de l'autre), faible pour la grenouille n° 1 (groupe des croix et groupe des points plus rapprochés), très faible pour le n° 3. On peut penser que, sur un grand nombre d'individus, il s'en trouverait sans doute quelques uns pour lesquels, à la limite, l'inhibition exercée par la vision sur les réactions vestibulaires postrotatoires serait à peu près nulle.

Ces résultats sont en accord avec ceux qu'ont obtenus les auteurs cités précédemment. Le mécanisme de l'inhibition des réactions postrotatoires par les stimulations visuelles est inconnu jusqu'à présent.

SUMMARY

In the frog has been studied the influence of vision upon the threshold of the vestibular postrotatory reactions (reactions elicited by the stimulation of the horizontal semi-circular canals). The stimulation was produced by stopping a uniform rotation in a very short time which allowed us to value the stimulation in terms of rotation speed. The experiments were carried out with frogs which first were able to see and then were blinded by section of the optic nerves. The threshold is the smallest rotation speed which is able to elicit a just visible reaction at the stopping of the rotation (slight movement of the head in direction of rotation) for each frog. It is greater when the animal is able to see than when it is blinded. It appears, therefore, that vision tends to inhibit the vestibular postrotatory reactions.

ZUSAMMENFASSUNG

Wir untersuchten beim Frosch den Einfluss des Sehens bei der Schwelle der postrotatorischen Vestibularreaktionen (Reaktionen, hervorgerufen durch die Reizung der semi-zirkularen horizontalen Kanäle). Die Reizung wird durch den Stillstand einer uniformen Rotation hervorgerufen. Im Stillstand, welcher in einem sehr kurzen Zeitraume realisiert wird, was uns erlaubt, den Wert der Stimulation in Form einer Rotationsgeschwindigkeit auszudrücken. Die Experimente wurden an Fröschen vorgenommen, welche zuerst ein Sehvermögen besassen, und darauf durch den Schnitt der optischen Nerven blind wurden. Für jeden der Frösche ist die Schwelle — die kleinste Rotationsgeschwindigkeit, welche fähig ist, beim Stillstand eine Reaktion zu verursachen, die gerade noch wahrnehmbar ist (leichte Bewegung des Kopfes in der Richtung der Rotation) — erhöhter, wenn das Tier sieht, als wenn es blind ist. Es erscheint infolgedessen, dass das Sehen die postrotatorischen Vestibularreaktionen zu verhindern neigt.

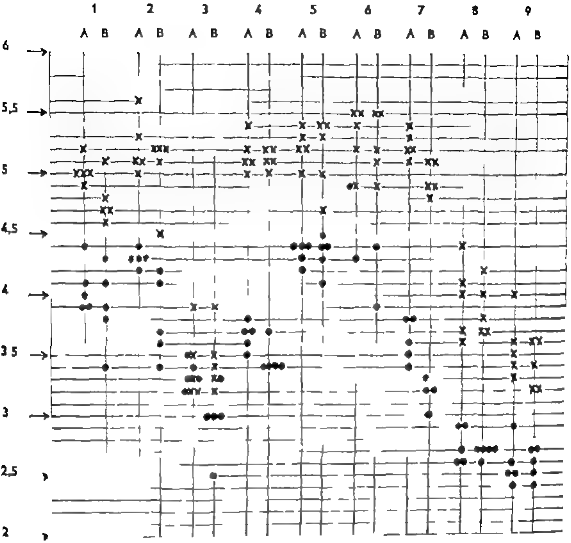

FIG. 1. *Horizontalement* : chiffres désignant les grenouilles (de 1 à 9) ; pour chacune d'elles, colonne A : rotation de sens horaire ; colonne B : rotation de sens antihoraire. *Verticalement* : vitesse de rotation, en degrés/seconde. Croix : seuils déterminés avant section des nerfs optiques ; cercles : seuils déterminés après section des nerfs optiques. (La grenouille n° 6 (non fixée) aveugle est morte en cours d'expérience. C'est pourquoi nous n'avons pu déterminer que 2 seuils journaliers chez cet animal.)

La figure 1 montre en outre que, à l'exception d'une seule grenouille (n° 3), le seuil journalier le plus élevé déterminé lorsque l'animal est privé de la vue est toujours inférieur au seuil journalier le plus bas déterminé lorsque le même animal voit. La différence entre ces deux valeurs est plus ou moins grande selon les animaux ; par exemple, elle est nettement plus importante pour les n°s 4, 7, 8 que pour les n°s 1, 2, 5, 9. Enfin, on peut voir que la grenouille n° 3 ne fait pas véritablement exception, puisque les deux groupes de valeurs des seuils journaliers ne se recouvrent que partiellement : l'ensemble des valeurs obtenues lorsque l'animal est aveugle reste inférieur à l'ensemble des valeurs obtenues lorsqu'il voit.

CONCLUSION

La vision, chez la grenouille, élève le seuil pour les réactions postrotatoires dues à la stimulation des canaux horizontaux la présence de la vue pendant et après la rotation, inhibe donc partiellement les réactions postrotatoires L'inhibition est plus ou moins marquée selon les individus, comme on peut le voir sur la figure par exemple, elle est importante pour la grenouille n° 7 (le groupe des croix et le groupe des points sont distants l'un de l'autre) faible pour la grenouille n° 1 (groupe des croix et groupe des points plus rapprochés) très faible pour le n° 3 On peut penser que, sur un grand nombre d'individus, il s'en trouverait sans doute quelques uns pour lesquels, à la limite, l'inhibition exercée par la vision sur les réactions vestibulaires postrotatoires serait à peu près nulle

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Reçue 21 décembre 1965

METABOLIC ACTIVITIES OF THE ENDOLYMPHATIC SAC

An Enzyme Histochemical and Autoradiographic Study

T. Ishii, H. Silverstein and K. Balogh Jr.

Boston, Mass., U.S.A.

From the Department of Otolaryngology (Head: Prof. H. F. Schuknecht) Massachusetts Eye and Ear Infirmary and the James Homer Wright Pathology Laboratories (Head: Prof. B. Castleman), Massachusetts General Hospital, Boston

The distribution of diphosphopyridine nucleotide diaphorase, triphosphopyridine nucleotide diaphorase, lactic dehydrogenase, malic dehydrogenase, succinic dehydrogenase, isocitric dehydrogenase, glucose-6-phosphate dehydrogenase and β-hydroxybutyric dehydrogenase, cytochrome oxidase, alkaline and acid phosphatase, leucine- and alanine-amino peptidase activity was demonstrated histochemically in the endolymphatic sac and in the perisaccular connective tissue. Enzyme activity was stronger in the epithelial cells lining the intermediate portion and in the cells floating free in the endolymph than in other parts of the sac, except for aminopeptidase activity which was marked in the perisaccular connective tissue too.

Foreign protein (peroxidase) was injected into the cochlear duct and after two days was found phagocytized in cells floating free in the endolymphatic sac but not in the lining cells themselves or elsewhere in the membranous labyrinth. Peroxidase was also observed in fibroblasts of the perisaccular connective tissue four days after injection.

Radioactive carbon labeled foreign protein was directly injected into the endolymphatic sac and visualized autoradiographically. Five minutes after injection radioactivity was seen only on the surface of the epithelial lining, but after 80 minutes survival there was radioactivity in the free-floating cells as well as in the epithelial lining cells and in the perisaccular tissue.

These observations are in agreement with the concept that endolymph flows from the cochlear duct to the endolymphatic sac, where proteins are phagocytized and/or transported by the lining epithelial cells into the perisaccular connective tissue. The endolymphatic sac is a metabolically active structure that functions as a filter for the membranous labyrinth.

This study was supported by Research Grants NB 04155-04 and 04093-01 from the National Institute of Neurological Diseases and Blindness, National Institutes of Health of the United States Public Health Service.

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Radioactive carbon labeled foreign protein was directly injected into the endolymphatic sac and visualized autoradiographically. Five minutes after injection radioactivity was seen only on the surface of the epithelial lining, but after 35 minutes survival there was radioactivity in the free-floating cells as well as in the epithelial lining cells and in the perisaccular tissue.

These observations are in agreement with the concept that endolymph flows from the cochlear duct to the endolymphatic sac, where proteins are phagocytized and/or transported via the lining epithelial cells into the perisaccular connective tissue. The endolymphatic sac is a metabolically active structure that functions as a filter for the membranous labyrinth.

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INTRODUCTION

Since Guild's (1927) original proposal that the endolymphatic sac may play an important role in the normal metabolic function of the inner ear evidence has been accumulating to support this concept Several investigators reported on the fate of dye or pigment injected into the cochlea and observed its accumulation in the endolymphatic sac (Guild 1927 Yamakawa 1929 Andersen 1948 Engstrom & Hjorth 1950) Recent electron microscopic studies (Lundquist Kimura & Wersall 1964 a 1964 b Lundquist, 1965) also confirmed Guild's observations Twenty four hours after the injection of colloidal silver into the cochlear duct at the basal turn Lundquist and collaborators (1964 a 1964 b 1965) found silver particles concentrated in macrophages within the lumen of the endolymphatic sac They also studied the ultrastructure of the epithelial cells lining the endolymphatic sac and found the cells of the intermediate portion to possess great pinocytotic activity consistent with this they observed numerous infoldings of the cytoplasmic membrane similar to those found in cells that are actively involved in fluid transport such as those of the kidney tubule ducts of the submaxillary salivary gland and ciliary body of the eye Silverstein (1966) analyzed the endolymph from the cochlea and from the endolymphatic sac and found in the latter high concentrations of total protein, lactic and malic dehydrogenase while the potassium level was low These findings suggest a filtering function for the endolymphatic sac Although surgical destruction of the endolymphatic sac produces no functional or histologic changes in monkeys (Lindsay 1947) and in cats (Lindsay *et al* 1952 Schuknecht & Kimura 1953 Schuknecht & Seifi 1963) in the guinea pig a marked endolymphatic hydrops develops after its removal (Kimura & Schuknecht 1965)

In order to study the functions of the endolymphatic sac at the cellular level an investigation was undertaken using histochemical techniques to demonstrate the presence of various enzymes within the lining cells of the endolymphatic sac and to localize foreign protein injected into the cochlear duct This study was supplemented by autoradiographic localization of radioactive protein injected into the endolymphatic sac

MATERIAL AND METHODS

Histochemical demonstration of enzyme activities

Twenty adult guinea pigs weighing 200–300 gm were anesthetized with ether then decapitated and their temporal bones removed The tissue blocks were decalcified for 14 days at 4 C with a 10% EDTA solution at pH 7 45 (Balogh 1962) The endolymphatic sac surrounded by a small block of decalcified bone was frozen on Dry Ice mounted and cut serially at 15 μ with a rotary microtome in a cryostat (−20 C) The sections were

mounted on clean coverslips and dried at room temperature for 30 minutes, then incubated in one of the various substrate solutions designed for demonstration of the activity of the following enzymes diphosphopyridine nucleotide diaphorase triphosphopyridine nucleotide diaphorase, lactic dehydrogenase malic dehydrogenase succinic dehydrogenase isocitric dehydrogenase glucose-6-phosphate dehydrogenase and β-hydroxybutyric dehydrogenase cytochrome oxidase alkaline and acid phosphatase leucine- and alanine-aminopeptidase Controls of the histochemical reactions were made by incubating sections in media from which the respective substrate had been omitted The techniques used for the demonstration of the oxidative enzymes were identical with those used before (Nomura & Balogh, 1964) Leucine and alamine-aminopeptidase activities were demonstrated with the methods of Nachlas *et al* (1957) and Burstone & Folk (1956) respectively For the localization of alkaline phosphatase activity adenosine triphosphate was used as substrate at pH 9 4 (Padykula & Herman 1955) Acid phosphatase activity was demonstrated in tissues that were fixed *in toto* in 4% formol-calcium solution (pH 7 1) at 4 C for 24 hours before decalcification The substrate solution was prepared according to Barka & Anderson (1962) and incubation carried out at *pH 5* All histochemical reactions were terminated by fixing the sections in 10% formalin finally the slides were mounted with Kaiser's glycerin jelly for light microscopic examination

Protein (peroxidase) uptake

In order to study the fate of proteins in the endolymphatic sac, horseradish peroxidase[1] was injected into the cochlear duct of 14 young adult albino guinea pigs. This foreign protein maintains its enzymatic activity after having been phagocytized and can be easily demonstrated histochemically (Straus, 1964 *a*, 1964 *b*) Following the intraperitoneal injection of nembutal (25 mg/kg) each tympanic bulla was exposed and opened from the ventral approach Using a sharp needle two small holes were made in the basal and third turns of the cochlea over the stria vascularis. About 1 μl of a horse-radish peroxidase solution (1 2 or 4% in physiological saline) was injected slowly with a micropipette into the third turn of the cochlear duct. Control animals were injected with Ringer's solution Afterwards, the holes in the cochlea were closed with bone wax. The animals were allowed to survive from one to four days then they were sacrificed under anesthesia, their temporal bones removed and fixed in 4% formol-calcium solution (pH 7 1) at 4 C for 24 hours. Decalcification and sectioning were according to the method described above Finally the injected peroxidase was demonstrated histochemically with the benzidine reaction (Straus, 1964 *a*, 1964 *b*)

[1] Horse-radish peroxidase (type II) Sigma Chemical Co St. Louis, Missouri

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F G 3. A i ph sphatase acti ity in the i t rmediat portio of the d lymphatic sa (a) Some cell are filled with zo dye depo it i dicating bundant en m acti ity where a thers show a weak re ction r n ne t II 580 (b) Acid pho phat se cti ity can be seen also in cell floating free in the nd lymph 470

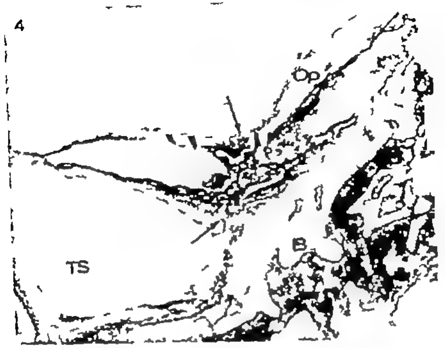

Fig. 4 Ala e-aminopeptidase acti ity is intense i the epithelial cell a d perisaccal connecti tissue (rrow) of the midportion. The free-floati g cell lso show considerable histochemical reaction. *Op* operculum; *TS*, tra erse i us; *B*, petrous bone with intense reaction f bone marrow cells. 68

(Fig. 6 a and b) However after 85 minutes survival C^{14}-labeled protein could be localized in the free-floating cells as well as in the epithelial lining cells of the intermediate portion of the sac, in the perisaccular macrophages and in th connective tissue (Fig 7) The distribution of the radioactive protein corresponded to that of peroxidase in the endolymphatic sac with the exception that peroxidase was not observed in the lining epithelial cells.

DISCUSSION

The findings of this study indicate that the lining cells of the endolymphatic sac contain enzymes which catalyze important metabolic processes. Most enzymes showed higher activities in the epithelial lining of the intermediate portion of the endolymphatic sac. All histochemical findings are consistent with the electron microscopic appearance of the lining cells (Lundquist, Kimura & Wersäll, 1964 *a*, 1964 *b* Lundquist, 1965) and suggest a higher metabolic activity in the lining cells of the mid-portion compared to other parts of the endolymphatic sac. Evidently the lining cells are capable of utilizing anaerobic as well as aerobic glycolysis for energy

FIG. 3. A l l ph phatase acti ity in the I t rmedi t porti of th nd lymphatic sa (a) Some cell are filled with az dye depo it indic ti g hi d t zyme acti it where thers show weak reaction or non at ll 580 (b) A ld phosphat se cti ity can be seen also in cells floating free i the ndolymph 470

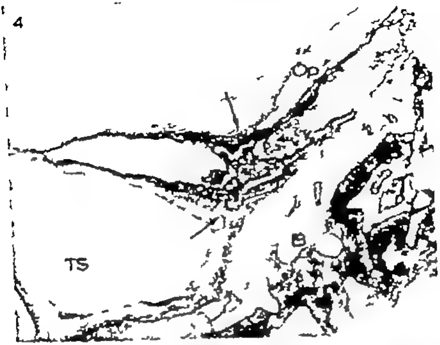

Fig. 4 Alanine-aminopeptidase activity is intense in the epithelial cells and perisaccular connective tissue (arrows) of the midportion. The free-floating cells also show considerable histochemical reaction. *Op* operculum; *TS* transverse sinus; *B*, petrous bone with intense reaction of bone marrow cells. ×56.

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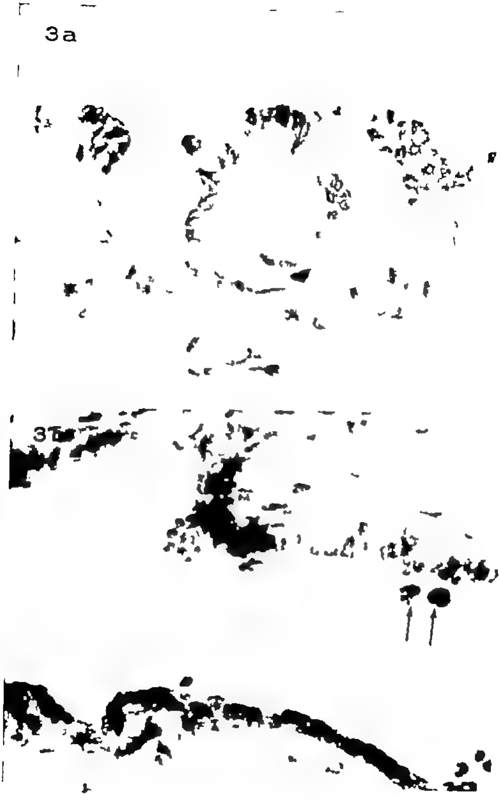

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in the perisaccular connective tissue cells is provided by the demonstration of marked aminopeptidase activity in these cells. Presumably the protein molecules or their break-down products eventually pass into the rich capillary network surrounding the endolymphatic sac.

The transport of foreign particles from the cochlear duct to the endolymphatic sac indicates a flow of endolymph in this direction and confirms Guild's observation (1927). Proteins that are normally concentrated in the endolymphatic sac probably are cleared by phagocytic activity of the free-floating macrophages as well as by transport via the lining epithelial cells into the surrounding perisaccular connective tissue. Probably this process is relatively slow as compared to the presumably rapid absorption of water that may be the cause of protein concentration in the endolymphatic sac. It appears from all the presented data that the endolymphatic sac is a metabolically active structure that functions as a filter for the membranous labyrinth.

ZUSAMMENFASSUNG

Die Verteilung der Diphosphopyridinnukleotid-Diaphorase, der Triphosphopyridinnukleotid-Diaphorase, der Laktat-Dehydrogenase, der Malat-Dehydrogenase, der Succinat-Dehydrogenase, der Isocitrat-Dehydrogenase, der Glukose-6-Phosphat-Dehydrogenase und der β-Hydroxybutyrat-Dehydrogenase sowie der Cytochromoxydase, der alkalischen und sauren Phosphatasen, der Leucin- und Alanin-Aminopeptidasen wurde im Saccus endolymphaticus und im perisacculären Bindegewebe histochemisch nachgewiesen. Die Enzymaktivität war in den Epithelzellen, die in der mittleren Zone liegen, und in den Zellen, die sich frei in der Endolymphe befinden, stärker als in anderen Teilen des Sackes. Hiervon ausgenommen war die Aminopeptidase, die auch im perisacculären Bindegewebe starke Aktivität zeigte.

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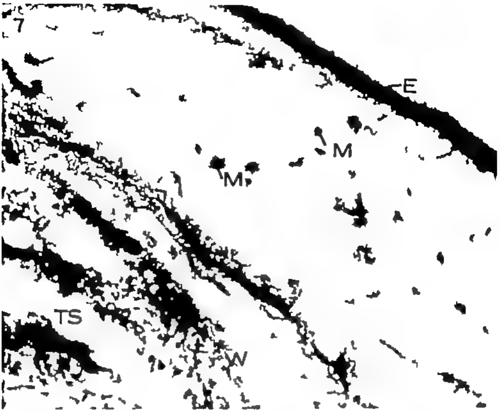

Fig 7 Autoradiograph showing C labeled protein 85 minutes after injection into the endolymphatic sac of a cat Radioactive protein is concentrated in the epithelial cells (*E*) in macrophages (*M*) and fibroblasts of the perisaccular connective tissue Silver granules are also seen in the wall (*W*) but not in the lumen of the transverse sinus (*TS*) ×280

Two days following injection into the cochlear duct, foreign protein (horse-radish peroxidase) was seen only in macrophages within the endolymphatic sac By the fourth day less peroxidase could be found in the macrophages however dark blue granules were then seen in the perisaccular connective tissue Since no peroxidase activity was found in the lining epithelial cells two days after injection it is probable that by that time this foreign protein has been completely taken up by macrophages and/or possibly carried through the wall of the endolymphatic sac into the surrounding connective tissue Similar observations were made by Lundquist *et al* (1964 *a* 1964 *b* 1965) who found silver particles engulfed by macrophages in the endolymphatic sac that were consequently carried through the epithelial lining into the perisaccular connective tissue

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The transport of foreign particles from the cochlear duct to the endolymphatic sac indicates a flow of endolymph in this direction and confirms Guild's observation (1927). Proteins that are normally concentrated in the endolymphatic sac probably are cleared by phagocytic activity of the free-floating macrophages as well as by transport via the lining epithelial cells into the surrounding perisaccular connective tissue. Probably this process is relatively slow as compared to the presumably rapid absorption of water that may be the cause of protein concentration in the endolymphatic sac. It appears from all the presented data that the endolymphatic sac is a metabolically active structure that functions as a filter for the membranous labyrinth.

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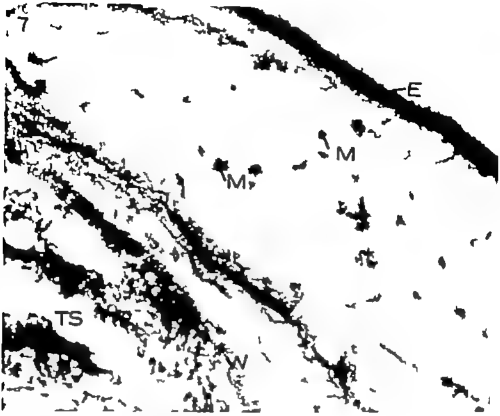

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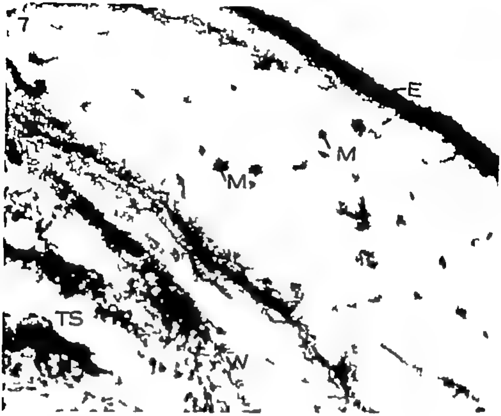

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Beide efferente olivo-cochleare Bündel, contralateral (COCB) und homolateral (HOCB) wurden an der Katze unter gleichartigen Bedingungen stimuliert In einigen Experimenten wurde jedes in seinem Ursprungskern stimuliert und in anderen an einem Punkt entlang der Bündelbahn Die gleichen Resultate wurden in beiden Reihen der Experimente erhalten Beide Bündel verursachen Aktions Potential(AP)-Senkung wobei das COCB ungefähr sechsmal stärker ist Die AP Senkung von beiden ist am grössten bei akustischer Stimulation von niedriger Frequenz und niedriger Intensität Im Gegensatz zur COCB-Stimulation wurde keine Veränderung im cochlearen Mikrophon Potential oder in der latenten Periode bei der HOCB-Stimulation beobachtet. Die Bedeutung dieser Resultate wird besprochen und es wird angenommen dass beide Bündel unabhängig voneinander funktionieren

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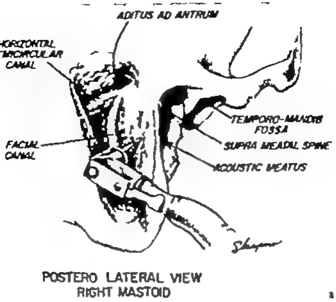
ADITUS AD ANTRUM
HORIZONTAL SEMICIRCULAR CANAL
FACIAL CANAL
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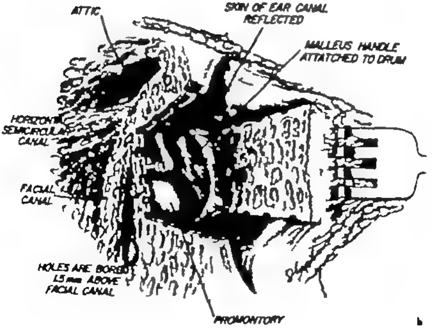
SUPRA MEATAL SPINE
ACOUSTIC MEATUS
POSTERO LATERAL VIEW
RIGHT MASTOID

a

Fig. 1


ATTIC
SKIN OF EAR CANAL REFLECTED
MALLEUS HANDLE ATTATCHED TO DRUM
HORIZONTAL SEMICIRCULAR CANAL
FACIAL CANAL
HOLES ARE BORED 1.5 mm ABOVE FACIAL CANAL
PROMONTORY

b

Fig. 2

A METHOD FOR PRESERVING THE POSTERIOR CANAL WALL AND BRIDGE IN THE SURGERY FOR CHOLESTEATOMA

Preliminary Report

A. LAPIDOT[1] and E. C. BRANDOW[2]

An operation is described which has been satisfactorily used in three patients and which we believe meets the requirements for the surgical management of cholesteatoma and chronic disease in the tympanic cleft.

There are essentially two conflicting schools of thought regarding the surgical management of cholesteatoma affecting the tympanic cleft.

Wullstein (1956) advocates the surgical creation of a mastoid cavity following the removal of the posterior canal wall. The latter insures adequate access to the entire tympanic cleft for the extirpation of the diseased tissue. The disadvantage of the procedure is that continued postoperative care is necessary and there is an associated limitation in aquatic sports.

Austin & Shea (1961), on the other hand, preserves the posterior canal wall and eliminates the establishment of a mastoid cavity. However, access to the entire tympanic cleft, particularly the facial recess, may be difficult at times when this technique is used. Consequently there is a percentage of recurrent disease. While this is a more difficult and challenging surgical procedure, the patient does not become an "aural cripple".

The work of Schnee (1963) was unknown to the senior author until the modification to be described in this paper was devised and clinically tried. Schnee described an osteoplastic flap technique whereby he included a portion of the posterior canal wall attached to the posterior canal skin by the use of two vertical osteotomies through and including the bridge. He further described additional tympano-meatal flaps for transmeatal access to the middle ear. We believe that the preservation of the bridge is important as a buttress and that no meatal incisions are necessary. The posterior canal wall is mobilised via two vertical and one horizontal osteotomy without disturbing the bridge.

OPERATIVE TECHNIQUE

Under local 2% Xylocaine-Adrenaline anesthesia the tympanic membrane is inspected transmeatally and the margins of the perforation are de-

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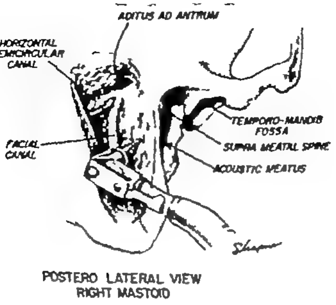
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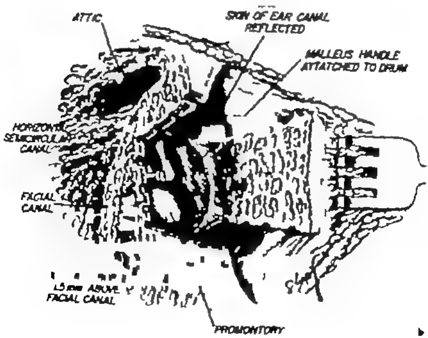
RIGHT MASTOID

FIG 1


ATTIC
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MALLEUS HANDLE ATTATCHED TO DRUM
HORIZONTAL SEMICIRCULAR CANAL
FACIAL CANAL
1.5 mm ABOVE FACIAL CANAL
PROMONTORY

FIG. 2.

A METHOD FOR PRESERVING THE POSTERIOR CANAL WALL AND BRIDGE IN THE SURGERY FOR CHOLESTEATOMA

Preliminary Report

A. LAPIDOT[1] and E. C. BRANDOW[2]

An operation is described which has been satisfactorily used in three patients and which we believe meets the requirements for the surgical management of cholesteatoma and chronic disease in the tympanic cleft.

There are essentially two conflicting schools of thought regarding the surgical management of cholesteatoma affecting the tympanic cleft.

Wullstein (1958) advocates the surgical creation of a mastoid cavity following the removal of the posterior canal wall. The latter insures adequate access to the entire tympanic cleft for the extirpation of the diseased tissue. The disadvantage of the procedure is that continued postoperative care is necessary and there is an associated limitation in aquatic sports.

Austin & Shea (1961), on the other hand, preserves the posterior canal wall and eliminates the establishment of a mastoid cavity. However, access to the entire tympanic cleft, particularly the facial recess, may be difficult at times when this technique is used. Consequently, there is a percentage of recurrent disease. While this is a more difficult and challenging surgical procedure, the patient does not become an "aural cripple".

The work of Schnee (1963) was unknown to the senior author until the modification to be described in this paper was devised and clinically tried. Schnee described an osteoplastic flap technique whereby he included a portion of the posterior canal wall attached to the posterior canal skin by the use of two vertical osteotomies through and including the bridge. He further described additional tympano-meatal flaps for trans-meatal access to the middle ear. We believe that the preservation of the bridge is important as a buttress and that no meatal incisions are necessary. The posterior canal wall is mobilised via two vertical and one horizontal osteotomy without disturbing the bridge.

OPERATIVE TECHNIQUE

Under local 2% Xylocaine-Adrenaline anesthesia the tympanic membrane is inspected transmeatally and the margins of the perforation are de-

[1] Chief Resident, Otolaryngology, Albany Medical Center Hospital ... Albany, N.Y., U.S.A. *Present address*: 17 ... Street, Bet Hakerem, Jerusalem, Israel.

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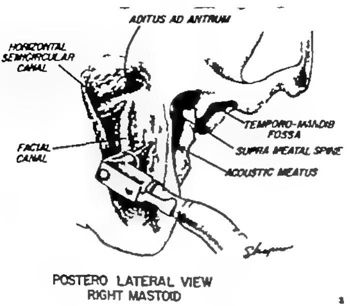
ADITUS AD ANTRUM
HORIZONTAL SEMICIRCULAR CANAL
FACIAL CANAL
TEMPORO-MANDIB FOSSA
SUPRA MEATAL SPINE
ACOUSTIC MEATUS
POSTERO LATERAL VIEW
RIGHT MASTOID

Fig. 1

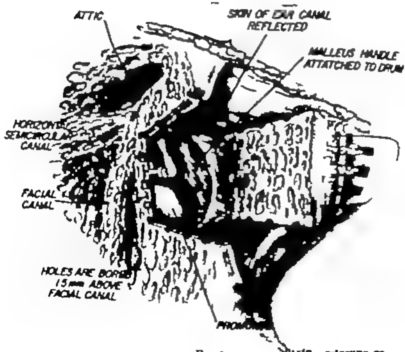
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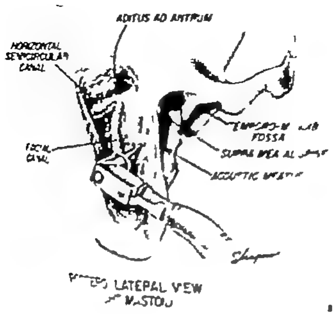
Fig. 2.


ADITUS AD ANTRUM
HORIZONTAL SEMICIRCULAR CANAL
FOSSA
LATERAL VIEW

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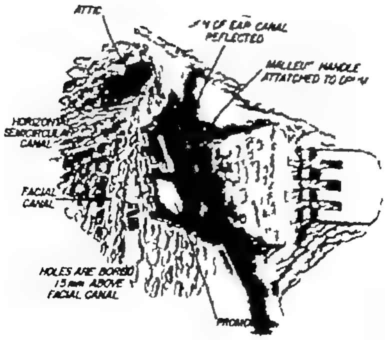
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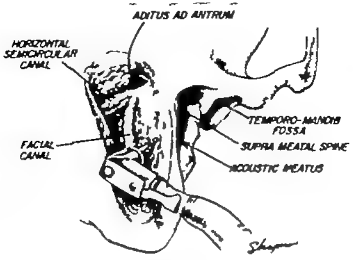
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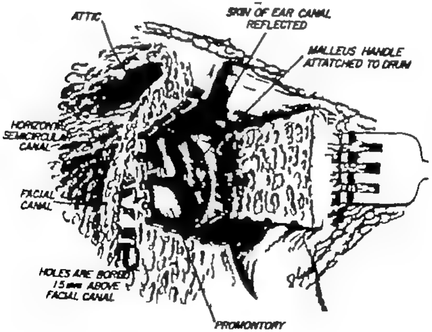
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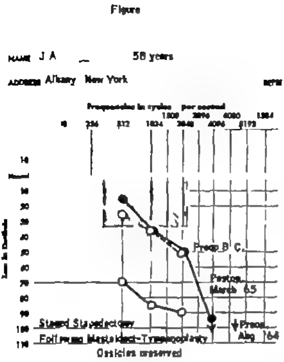


FIG 3 *a*

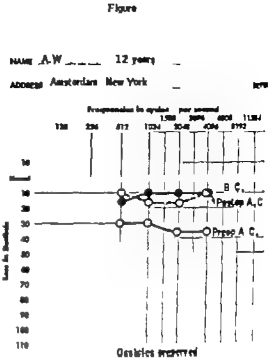


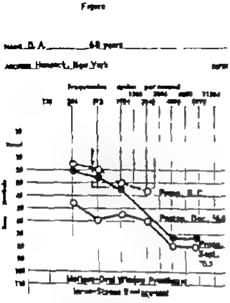
FIG 3 *b*

epithelialised (Austin & Shea 1961) As much as possible of the cholesteatoma sac is removed through the perforation At the completion of this stage, endotracheal fluothane anesthesia is commenced

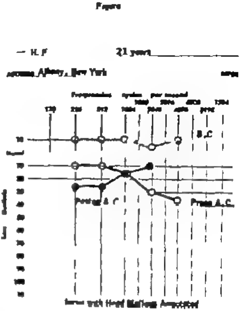
A postauricular incision is made and a simple mastoidectomy atticotomy performed The posterior canal wall is thinned from behind to approximately 1 0–1.5 mm using a drill (compressed air or motor driven) A vertical osteotomy is made just below the level of the superior buttress using a small 1 mm rosehead burr from the lateral free margin of the posterior canal A similar parallel osteotomy is made inferiorly at approximately the level of the floor of the external canal The two osteotomies are then connected by an horizontal osteotomy approximately 1–2 mm above the facial ridge (Fig 1) The isolated bone fragment is elevated anteriorly in continuity with the canal skin and tympanic membrane leaving the posterior portion of the bridge intact (Fig 2)

The indicated attic and middle ear surgery is carried out while retracting the bone-skin tympanic flap Further annular and attic bone may be burred away anteriorly or posteriorly for good visualization The cholesteatomatous sac may be delivered posteriorly or anteriorly whichever is preferred to maintain continuity

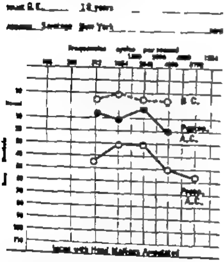
If adequate removal of the cholesteatoma is possible with preservation of ossicles, this is done (Fig 3 *a*) However amputation of the head of the malleus is no deterrant to the subsequent restoration of hearing with a malleus-oval window wire prosthesis (Fig 4) or as a myringo-stapedlopexy



F 4 a.



F 4 b



F a. 4

(Fig. 4 *b* and *c*) Repair of the drum defect is made with a fascial graft slid forward from behind the aditus, and a rotated muscle flap may be inserted into the mastoid cavity The canal skin-bone flap is repositioned and the canal packed with small pieces of gelfoam

DISCUSSION

There are a number of advantages of this technique Good visualization is afforded f the hypotympanum facial recess and attic, despite preservation

and ossicles and on cortical bone from the diaphysis of long cylindrical, human bones They revealed areas of necrobiosis and necrosis in the enchondral layer their presence being of importance we believe in the etio-pathogenesis of otosclerosis, a subject on which we are also working

MATERIAL AND METHOD

Studies were made of

(a) Otic capsules from individuals aged 18 to 80 years (50 specimens)
(b) Fragments of capsule obtained from a fenestration operation for otosclerosis (1 specimen)
(c) Stapes, obtained from operations and autopsies (10 specimens) malleus obtained from operations and autopsies (4 specimens) incus, obtained from operations and autopsies (4 specimens)
(d) Three canine otic capsules, two from sheep five from rabbits and one from a cat
(e) Six fragments of human tibial and femoral diaphysis obtained from amputations due to bone tumours and senile gangrene

The sections were stained by the following techniques Hematoxylin eosin Wilder s, and Mallory s hematoxylin phosphotungstic acid method

In frozen sections, obtained after decalcifying in 5 % trichloroacetic acid solution the presence of lipids was studied in the osteocytes, Sudan black and Sudan IV being used for his purpose In some paraffin wax sections the presence of desoxyribonucleic acid (Feulgen) and or mucopolysaccharides (PAS) was studied

RESULTS

The enchondral layer of human auditory capsule always shows cartilaginous islets surrounded by lamellas bone with few Haversian systems, in which the lumen of many of the blood vessels is obliterated (Figs 1 2 and 3)

In many areas the nuclei of the osteocytes are pycnotic or absent and

F 1 N rmal hum otl psul In rea f the ncho dral l er l whi l the blit rati seen in ma y f tl blood es ls, w ll xt l re f mpty o teopl t (cer sed bo l ssue) H.F 60

Fig. 3 Tra rs secti f a H ersia ca l urrou ded by mpt l cu cept l th immed at l init f the blood sel H.F 650

Fig. 4 A part of th stapes h wi g rea f bo tiss dev id f l l l th osteopl t H F 160

Fig. 5 En l dral l yer howi g osteopl t filled with red t l ed f t (l ll k th p l re) d otl ld area f bo with mpt lacu S da IV 160

Fig. 7 A fragme t f the h ndral la er bt l ed from f estrati f ot scl r l Numerou mpty l cun can be ee H.E. 23

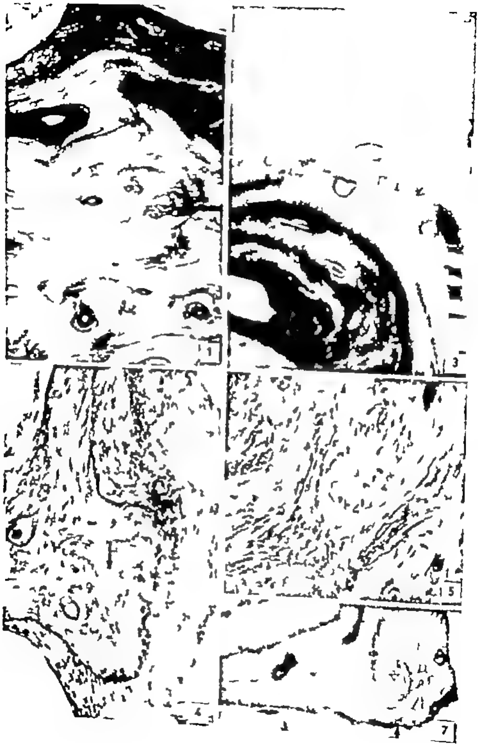

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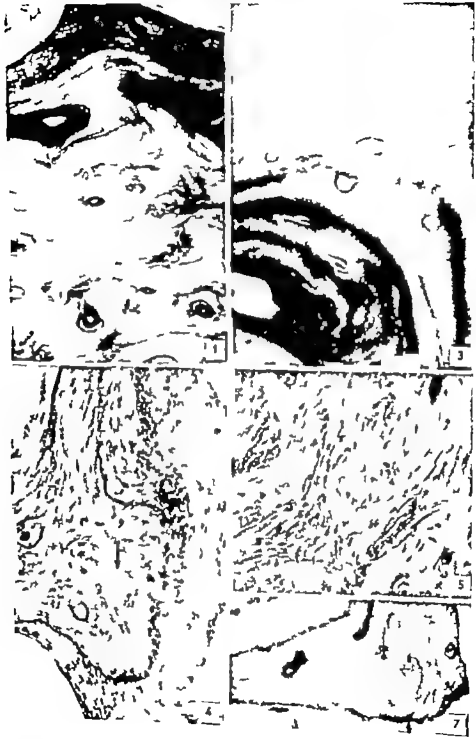
Fig. 3 Tra rse secti n f a Ha ersia c n l urrou led l y mpt l cu cept l tl mmed t l inity f the blood essel H E 650

F 4 A part f th tapes howing re f bone tiss d ld f l l l ll teo- pl t H.E. 160

Fig. 5 En h ndral l yer sh wing teopl t filled with red st l ed f t (l ll k l (th plct re) a d ther ld area f bo with mpty lacu Sud IV 160

F 7 A fragme t f th h dral la er btai ed from f estrati f tosel n l Numerou mpty lacu n be seen H.E. 25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F G. 3 Tra s rse ecti n of a H ersi nal surro n led l mpt l a cept in th immediat vici ity f th blood sel H F 630

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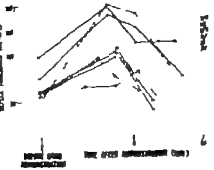


Fig. 1. Reflex threshold prior to and following administration of 6 mg d-t. bocurarine.

Results

In Fig. 1 are plotted thresholds for each subject prior to injection of the drug and at specified intervals thereafter. The average reflex threshold was approximately 94 dB. Following injection of the drug, the thresholds increased, the peak increase occurring between 3 and 10 minutes after injection. Every subject evidenced an appreciable increase in threshold. The average peak increase observed was approximately 12 dB.

EXPERIMENT II. TTS FOLLOWING NOISE EXPOSURE

A. Low Frequency TTS

The major effects of AR action, according to Galambos & Rupert (1959), Simmons (1960) and others, are at low frequencies. The decision was made first to measure TTS with and without curare following exposure to intermittent fairly low frequency (600–1200 cps, 110 dB) noise.

The noise was generated by feeding the output of a Grason Stadler noise generator through a Krohn-Hite filter set at a nominal 600–1200 cps band pass, into a Beyer earphone. (Sound pressure level was measured in a 6 cc ASA coupler with a model 4132 Brüel and Kjaer microphone.) In order to minimize the possibility of reflex adaptation the noise was abruptly interrupted for 3 seconds following each 27 seconds of exposure. Total duration of exposure (including the 3 seconds off periods) was 10 minutes. Exposure was initiated 30 seconds after injection. According to the data of Experiment I, drug action should have been maximal approximately [illegible] minutes after injection. Therefore a 10 minute exposure period initiated 30 seconds after drug injection should have been symmetrically distributed around the time of peak action.

Thresholds were measured before exposure by having subjects track their thresholds on a Grason Stadler recording attenuator fed by a Krohn-Hite oscillator for 25 seconds at each of four test frequencies: 1000, 2000, 4000 and 6000 cps. Post-exposure thresholds were measured 90 seconds

control conditions. In the present study, four sets of experiments were conducted. Each involved the administration of light to moderate doses (6–8 mg) of a form of curare (*d*-tubocurarine) and the measurements of auditory effects. The experiments described in the present paper include (1) measurements of change in AR threshold, (2) measurement of TTS produced by relatively low frequency noise and higher frequency noise, (3) measurement of contralateral remote masking by noise and tones, and (4) measurement of ipsilateral remote masking by tones.

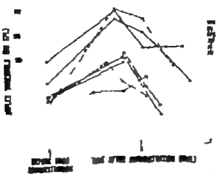
EXPERIMENT I. MEASUREMENT OF AR ACTION

It is possible to obtain relatively reliable AR thresholds by employing the acoustic impedance bridge devised by Zwislocki (1961), and moreover, this procedure for measurement of AR action is similar to that employed by Lehnhardt (1959). Accordingly, this device was employed for threshold determination in this experiment.

Procedure

Several volunteer observers were given *d*-tubocurarine administered intravenously over a 30 sec period. Those weighing less than 175 lbs were given 6 mg; those exceeding that weight, 8 mg. These dosages produced marked diplopia and reductions in grip strength of 45–95%. Thresholds for the reflex were measured with the Grason-Stadler Zwislocki acoustic bridge. With this device an electroacoustic transducer radiates sinusoidal sounds equal in amplitude but opposite in phase into the ear and into a tube of variable acoustic resistance and capacitance. The reflected sounds are brought back to the ear of the operator. The operator listens to the output and adjusts the variable components of acoustic impedance until the sound reaches a minimal level. At this point the variable components are equal in acoustic resistance and reactance to that of the ear (Zwislocki, 1961). When the reflex is activated, the acoustic impedance of the ear is altered so that the reflected sound from the ear and the variable components in the device are no longer equal. The reflected sounds from these two sources no longer cancel one another and thus while the reflex is operating the tone becomes louder. The probe tone employed was 250 cps.

The noise employed to elicit the reflex was produced by feeding the output of a Model 349 Allison equalizer (with noise generator incorporated) through a Hewlett Packard decade attenuator into a Beyer insert earphone. The equalizer was set to pass maximally those frequencies between 1200 and 4800 cps; above and below these values attenuation was set at maximum (normally greater than 40 dB). Intensity of sound in the phone was measured in a 2cc Brüel and Kjaer coupler with a model 3141 Brüel and Kjaer microphone. It was varied by adjusting a decade attenuator in both ascending and descending methods of limit series in order to obtain reflex threshold.



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in the individual subject. Of the total 68 subjects, 54 were tested with one acceleration series, 12 with two different series, and 2 with three series. The subjects tested for more than one strength of stimulus rested for about 30 min. without the mask between each series of accelerations. This was regarded as adequate since they seemed to be completely alert and unfatigued during the whole duration of the recordings.

Statistical analyses

The results in each group are listed in Table 1. Each vertical column represents an individual series of 5 accelerations. The following calculations were made in each series:

(1) The arithmetic mean $\bar{X}$. This is a direct expression of the subject's latency time level at the given strength of stimulus.

(2) The standard deviation $\hat{S}$ expresses the variation in the latency times. The calculation was made according to the equation

$$\hat{S} = \sqrt{\frac{\Sigma(X_i - \bar{X})^2}{n-1}}$$

in which Σ is the sum, $\Sigma(X_i - \bar{X})^2$ is the sum of the squares of the differences between each latency time recorded (X_i) and the arithmetic mean ($\bar{X}$) of the latency times, and n is the number of measurements, in this case 5.

(3) The ratio of the standard deviation to the arithmetic mean in each subject was calculated. The coefficient of variation $C(\hat{S}/\bar{X})$ obtained in this way is also given in the table.

(4) The arithmetic means, standard deviations and coefficients of variation were also calculated by groups for the latency times in the first 12 stimulations, the second 12, third 12, and so on (horizontally in the tables). These values are given in the right hand columns of Table 1.

RESULTS

A survey of the results shows that in the majority of cases, the arithmetic mean of the latency time decreased with rising strength of stimulus. Although the standard deviation varies in the different groups, a tendency to a decrease can be noted at high speeds of acceleration. The relative standard deviation within the groups, expressed as the coefficient of variation, seems to be well collected around the value 0.4. If the individual results in the respective groups are studied, large variations are seen both within the group and in the individual subject. Some concentration is, however, found around a mean value characteristic of each strength of stimulus.

In general, the results differed greatly in the various subjects. Thus in some there were large variations from one recording to the next, whereas

in others the latency times showed a distinct regularity As could be expected, the variations were greatest in those groups in which the stimulus was weak at high accelerations, on the other hand, fairly good reproducibility could be noted from one experiment to the next The mean values for the 12 subjects in the group in each acceleration experiment are given on the right-hand side in Table 1 It is seen that in groups 1 and 2, the arithmetic mean for all subjects increased slightly from recording 1 to recording 3 inclusively No such change occurred in the other groups.

If a comparison is made between the standard deviation for all subjects (Table 1 right hand side) and the corresponding value in the individual subjects, it is found that the deviation is consistently much larger in the former case than in the latter This also applies to the coefficient of variation

Group 6 differed somewhat from the other groups in that its arithmetic means was 6.8 sec In the other groups, a continuous decrease in the arithmetic mean was noted whereas in this group there was thus a transient increase.

DISCUSSION

The mechanism underlying the nystagmus reaction is highly complicated, and is still largely unelucidated. It has proved to be influenced by several centres in the central nervous system As an expression of this circumstance the present study has shown poor reproducibility of the reaction at any rate at low strengths of stimulus Here, the standard deviation is large whereas it shows a tendency to decrease with rising strength of stimulus Nevertheless, the individual values in all groups are collected within a relatively narrow range, characteristic of each strength of stimulus Even if the absolute standard deviation is large, the relative standard deviation expressed as the coefficient of variation—is practically the same in all groups. This implies that the distribution is by no means completely random.

In groups 1 and 2, the arithmetic mean of the latency time rose from experiment 1 to experiment 3 Since this series, with a low speed of acceleration, took considerably longer than with high speeds of acceleration, it is conceivable that the subjects might have become tired A study of the individual results nevertheless discloses no such tendency Thus, the latency times were scattered completely at random during the whole experimental series. A superficial analysis might interpret the prolongation of the latency time as an expression of habituation However since no change similar to that in groups 1 and 2 can be detected in the other groups with much higher strengths of stimulus, this possibility can be ruled out. Moreover it can be questioned whether the variations in the arithmetic means listed on the right hand side of Table 1 are in fact, of such an order of magnitude that any conclusions whatsoever can be drawn

in the individual subject. Of the total 68 subjects 54 were tested with one acceleration series, 12 with two different series, and 2 with three series. The subjects tested for more than one strength of stimulus rested for about 30 min without the mask between each series of accelerations. This was regarded as adequate since they seemed to be completely alert and unfatigued during the whole duration of the recordings.

Statistical analyses

The results in each group are listed in Table 1. Each vertical column represents an individual series of 5 accelerations. The following calculations were made in each series:

(1) The arithmetic mean $\bar{X}$. This is a direct expression of the subject's latency time level at the given strength of stimulus.

(2) The standard deviation $\hat{S}$ expresses the variation in the latency times. The calculation was made according to the equation

$$\hat{S} = \sqrt{\frac{E(X_i - \bar{X})^2}{n-1}}$$

in which E is the sum. $F(X_i - \bar{X})^2$ is the sum of the squares of the differences between each latency time recorded (X_i) and the arithmetic mean ($\bar{X}$) of the latency times, and n is the number of measurements, in this case 5.

(3) The ratio of the standard deviation to the arithmetic mean in each subject was calculated. The coefficient of variation $C(\hat{S}/\bar{X})$ obtained in this way is also given in the table.

(4) The arithmetic means, standard deviations and coefficients of variation were also calculated by groups for the latency times in the first 12 stimulations, the second 12, third 12 and so on (horizontally in the tables). These values are given in the right hand columns of Table 1.

RESULTS

A survey of the results shows that in the majority of cases, the arithmetic mean of the latency time decreased with rising strength of stimulus. Although the standard deviation varies in the different groups, a tendency to a decrease can be noted at high speeds of acceleration. The relative standard deviation within the groups, expressed as the coefficient of variation, seems to be well collected around the value 0.4. If the individual results in the respective groups are studied, large variations are seen both within the group and in the individual subject. Some concentration is, however, found around a mean value characteristic of each strength of stimulus.

In general the results differed greatly in the various subjects. Thus in some there were large variations from one recording to the next, whereas

in others the latency times showed a distinct regularity. As could be expected, the variations were greatest in those groups in which the stimulus was weak; at high accelerations, on the other hand, fairly good reproducibility could be noted from one experiment to the next. The mean values for the 12 subjects in the group in each acceleration experiment are given on the right-hand side in Table I. It is seen that in groups 1 and 2, the arithmetic mean for all subjects increased slightly from recording 1 to recording 5 inclusively. No such change occurred in the other groups.

If a comparison is made between the standard deviation for all subjects (Table I, right-hand side) and the corresponding value in the individual subjects, it is found that the deviation is consistently much larger in the former case than in the latter. This also applies to the coefficient of variation.

Group 6 differed somewhat from the other groups in that its arithmetic means was 6.8 sec. In the other groups, a continuous decrease in the arithmetic mean was noted, whereas in this group there was thus a transient increase.

DISCUSSION

The mechanism underlying the nystagmus reaction is highly complicated, and is still largely unelucidated. It has proved to be influenced by several centres in the central nervous system. As an expression of this circumstance, the present study has shown poor reproducibility of the reaction, at any rate at low strengths of stimulus. Here the standard deviation is large, whereas it shows a tendency to decrease with rising strength of stimulus. Nevertheless, the individual values in all groups are collected within a relatively narrow range, characteristic of each strength of stimulus. Even if the absolute standard deviation is large, the relative standard deviation, expressed as the coefficient of variation—is practically the same in all groups. This implies that the distribution is by no means completely random.

In groups 1 and 2, the arithmetic mean of the latency time rose from experiment 1 to experiment 5. Since this series, with a low speed of acceleration, took considerably longer than with high speeds of acceleration, it is conceivable that the subjects might have become tired. A study of the individual results nevertheless discloses no such tendency. Thus, the latency times were scattered completely at random during the whole experimental series. A superficial analysis might interpret the prolongation of the latency time as an expression of habituation. However, since no change similar to that in groups 1 and 2 can be detected in the other groups with much higher strengths of stimulus, this possibility can be ruled out. Moreover, it can be questioned whether the variations in the arithmetic means listed on the right hand side of Table I are, in fact, of such an order of magnitude that any conclusions whatsoever can be drawn

in the individual subject. Of the total 68 subjects, 54 were tested with one acceleration series, 12 with two different series, and 2 with three series. The subjects tested for more than one strength of stimulus rested for about 30 min without the mask between each series of accelerations. This was regarded as adequate since they seemed to be completely alert and unfatigued during the whole duration of the recordings.

Statistical analyses

The results in each group are listed in Table 1. Each vertical column represents an individual series of 5 accelerations. The following calculations were made in each series:

(1) The arithmetic mean $\bar{V}$. This is a direct expression of the subject's latency time level at the given strength of stimulus.

(2) The standard deviation $\hat{S}$ expresses the variation in the latency times. The calculation was made according to the equation

$$\hat{S} = \sqrt{\frac{\Sigma (V_1 - \bar{V})^2}{n-1}}$$

in which Σ is the sum, $\Sigma (V_1 - \bar{V})^2$ is the sum of the squares of the differences between each latency time recorded (V_1) and the arithmetic mean ($\bar{V}$) of the latency times, and n is the number of measurements, in this case 5.

(3) The ratio of the standard deviation to the arithmetic mean in each subject was calculated. The coefficient of variation $C(\hat{S}/\bar{V})$ obtained in this way is also given in the table.

(4) The arithmetic means, standard deviations and coefficients of variation were also calculated by groups for the latency times in the first 12 stimulations, the second 12, third 12, and so on (horizontally in the tables). These values are given in the right hand columns of Table 1.

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A survey of the results shows that in the majority of cases, the arithmetic mean of the latency time decreased with rising strength of stimulus. Although the standard deviation varies in the different groups, a tendency to a decrease can be noted at high speeds of acceleration. The relative standard deviation within the groups, expressed as the coefficient of variation seems to be well collected around the value 0.4. If the individual results in the respective groups are studied, large variations are seen both within the group and in the individual subject. Some concentration is, however, found around a mean value characteristic of each strength of stimulus.

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If a comparison is made between the standard deviation for all subjects (Table 1, right hand side) and the corresponding value in the individual subjects, it is found that the deviation is consistently much larger in the former case than in the latter. This also applies to the *coefficient of variation.*

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DISCUSSION

The mechanism underlying the nystagmus reaction is highly complicated, and is still largely unelucidated. It has proved to be influenced by several centres in the central nervous system. As an expression of this circumstance, the present study has shown poor reproducibility of the reaction, at any rate at low strengths of stimulus. Here the standard deviation is large, whereas it shows a tendency to decrease with rising *strength* of stimulus. Nevertheless, the individual values in all groups are collected *within* a relatively narrow range, characteristic of each strength of stimulus. Even if the absolute standard deviation is large, the relative standard deviation—expressed as the coefficient of variation—is practically the same in all groups. This implies that the distribution is *by* no *means* completely random.

In groups 1 and 2, the arithmetic mean of the latency time *rose from experiment* 1 to experiment 5. Since this series, with a low speed of *acceleration*, took considerably longer than with high speeds of acceleration, it is *conceivable that the subjects* might have become tired. A study of the individual results, nevertheless, discloses no such tendency. Thus, the latency times were scattered *completely at random* during the whole experimental series. A superficial analysis might interpret the prolongation of the latency time as an expression of habituation. However, since no change similar to that in *groups 1 and 2* can be detected in the other groups with much higher strengths of stimulus, this possibility can be ruled out. Moreover, it can be *questioned* whether the variations in the arithmetic mean, listed on the right hand side of *Table 1* are, in fact, of such an order of magnitude that any conclusion whatsoever can be drawn.

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Statistical analyses

The results in each group are listed in Table 1 Each vertical column represents an individual series of 5 accelerations The following calculations were made in each series

(1) The arithmetic mean $\bar{Y}$ This is a direct expression of the subject's latency time level at the given strength of stimulus

(2) The standard deviation $\hat{S}$ expresses the variation in the latency times The calculation was made according to the equation

$$\hat{S} = \sqrt{\frac{F(Y_1 - \bar{Y})^2}{n-1}}$$

in which F is the sum $F(Y_1 - \bar{Y})^2$ is the sum of the squares of the differences between each latency time recorded (Y_1) and the arithmetic mean ($\bar{Y}$) of the latency times, and n is the number of measurements in this case 5

(3) The ratio of the standard deviation to the arithmetic mean in each subject was calculated The coefficient of variation $C(\hat{S}/\bar{Y})$ obtained in this way is also given in the table

(4) The arithmetic means, standard deviations and coefficients of variation were also calculated by groups for the latency times in the first 12 stimulations, the second 12 third 12, and so on (horizontally in the tables) These values are given in the right hand columns of Table 1

RESULTS

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eintrat, erscheint aber sicher, dass die Naphtholacetat Reaktion im wesentlichen Esterasen nachweist.

Der histochemische Nachweis von Lipasen nach Gomori (1952) ist aus vielerlei Gründen problematisch. Die Überschneidungen des Wirkungsbereichs von Esterasen und Lipasen sind schon erwähnt worden. In dieser Hinsicht bietet die Inaktivierung mancher Esterasen durch Gallensalze bei gleichzeitiger Aktivierung von Lipasen eine wertvolle Hilfe bei der Unterscheidung beider Fermentklassen. In der Tat sieht man beim Esterasenachweis unter gleichzeitiger Zugabe von Natriumtaurocholat eine Abnahme der Reaktionsstärke, was insoweit für die Esterasenatur der nachgewiesenen Substanzen spricht. Der Nachweis von Lipasen mit der Tween Methode ist aber noch mit anderen Unsicherheiten behaftet. Wie erwähnt wird Tween 60 auch von Esterasen hydrolysiert, Tween 80 dagegen kaum. Ein entscheidender Vorteil der Tween Substrate ist andererseits ihre Wasserlöslichkeit. Die handelsüblichen Tween Substrate enthalten jedoch schon geringe Mengen freier Fettsäuren durch spontanen Abbau der Tweens. Außerdem sind Fettsäuren oft im untersuchten Gewebe vorhanden, hier zw. nicht frei, sondern meist als Kalkseifen gebunden. Der histochemische Lipasenachweis beruht nun auf der Abspaltung von Fettsäuren aus dem Tween Substrat durch die Lipasewirkung bei gleichzeitiger Bildung von Calciumseifen durch den $CaCl_2$-Gehalt der Inkubationslösung. Die Kalkseifen werden dann sekundär durch Bleinitrat in Bleiseifen verwandelt, welche durch Ammoniumsulfid in braunschwarze Bleisulfidkörnchen überführt werden. Der zweite Teil der Reaktion erfasst zwangsläufig auch Salze von Fettsäuren, welche bereits im Gewebe vorhanden waren und welche nicht erst durch Lipasewirkung von den Tweens abgespalten wurden. Dies gilt vor allem für lipidreiche Gewebsorte wie z. B. die Nervenscheiden im Modiolusbereich. Hier liegen Fettsäuren vor, die teilweise auch erst nach Formoleinwirkung aus grösseren Lipidmolekülen entstanden sein mögen und die vom Gomori Nachweis wie auch vom Holczinger Nachweis gleichermassen erfasst werden. So wird es verständlich, dass zwischen Fettsäure-Reaktion nach Formolfixierung und Tween 80-Inkubation mit Kupferacetat und Rubeanwasserstoffsäure an unserem Material nur geringe Unterschiede auftraten. Der „Lipase" Nachweis ist eben unter diesen Umständen teilweise ein Nachweis von Fettsäuren bzw. deren Seifen, welche unter Formoleinwirkung aus Lipiden entstanden sind.

Auch beim üblichen Lipasenachweis mit Tweens und Calcium-Bleinitrat Ammoniumsulfid muss sen unspezifische Reaktionen abgegrenzt werden. Zunächst weist Tween 60 — wie von anderem Material bekannt — auch in der Cochlea teilweise unspezifische Esterasen nach. Dafür spricht insbesondere die partielle Hemmung der Reaktion nach Natriumtaurocholat, welches Lipasen immer nur aktiviert, nie jedoch hemmt. Cholinesterasen konnten allerdings durch die ungehemmte Reaktion nach Eserin ausgeschlossen werden. Die partielle Hemmung nach DFP könnte den Lipaseanteil darstellen, da nach Gomori & Chessick (1953) auch Lipasen durch DFP gehemmt wer-

spalten. Die Abtrennung unspezifischer Esterasen von Lipasen erfolgt also methodisch nur teilweise vom Substrat her. Immerhin soll nach Gomori (1949) das *Tween 80*-*Substrat* (Ölsäureester des Polymannitol, also mit ungesättigter Fettsäure) für Lipase spezifisch sein, während Tween 60 (Stearinsäureester von *Polymannitol*) von Esterasen und Lipasen hydrolysiert wird. Eine weitere Unterscheidung von Esterase und Lipase erfolgt durch Gallensalze, wobei Natriumtaurocholat die Lipase aktiviert, die Esterase dagegen hemmt (Barrnett & Seligman 1951). Einzelne Esterasen sollen allerdings auch durch Natriumtaurocholat aktiviert werden.

Innerhalb der unspezifischen Esterasen kann man heute histochemisch 3 Typen unterscheiden (vgl. hierzu Pearse 1961), die Esterasen A, B und C. Der Typ B wird Diisopropylfluorophosphat (DFP) in einer Konzentration von 10[illegible] M gehemmt, A und C jedoch nicht. Typ A wird ausserdem vom Natriumsalz des *p*-Hydroxymercuribenzoats (früher als *p*-Chloromercuribenzoat angesehen) gehemmt, während Typ C aktiviert wird. Die Abtrennung von Cholinesterasen einschliesslich der Acetylcholinesterase von einfachen Esterasen gelingt leicht durch DFP oder Eserin (Physostigmin), welche beide die Cholinesterasegruppe inaktivieren.

Zum Nachweis von Esterasen bedienten wir uns der Methode nach Burstone (1957). Dabei wird durch die Esterasewirkung das Naphthol AS-D acetat aufgespalten und der substituierte Naphtholrest mit einem Diazoniumsalz zu einem blauen oder rotblauen Azofarbstoff an den Stellen der Gewebsaktivität gekuppelt. Der negative Ausfall der Reaktion bei Weglassen des Substrats bzw. des Diazoniumsalzes zeigt, dass keine Niederschlagsbildung des Diazoniumsalzes bzw. keine unspezifische Bindung des Naphtholderivates vorgekommen ist. Die als positiv beschriebenen Stellen enthalten somit Esterase. Bei Zusatz von Eserin zur Inkubationslösung ändert sich das Bild nicht. Es handelt sich also bei den von uns nachgewiesenen Substanzen nicht um Pseudocholinesterase oder Acetylcholinesterase. Diese Fermente sind zwar auch in der Lage, einfache Naphtholester zu spalten, werden jedoch durch einen Zusatz von Eserin 10^{-5} M völlig gehemmt. Bei Zusatz von DFP in einer Konzentration von 10^{-3} M ergab sich nur eine geringe Abnahme der Reaktionsstärke. Auch hierdurch kann man Cholinesterasen weitgehend ausschliessen. Die mässige Abnahme der Reaktionsintensität nach DFP darf wohl auf den B-Typ unspezifischer Esterasen bezogen werden, da dieser durch das organische Phosphat inaktiviert wird. Neben einer geringen Menge von B-Esterase lagen somit hauptsächlich Esterasen vom Typ A oder C vor. Nach Behandlung mit *p*-Hydroxymercuribenzoat fiel die Esterase-Reaktion eher intensiver aus. Es liegen somit neben B-Esterasen hauptsächlich C-Esterasen vor. Bei Natriumtaurocholat-Zusatz wurde die Esterase-Reaktion nur partiell gehemmt. Während der gehemmte Anteil sicher auf Esteraseaktivität zurückzuführen ist, muss es bei dem ungehemmten Anteil *fraglich bleiben*, wieweit Lipase oder taurocholataktivierte Esterase dafür verantwortlich ist. Da nach DFP das die Lipasen hemmt, nur eine geringfügige Abnahme der Reaktionsstärke

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Auch beim üblichen Lipasenachweis mit Tweens und Calcium-Bleinitrat-Ammoniumsulfid müssen unspezifische Reaktionen abgegrenzt werden. Zunächst weist Tween 60 — wie von anderem Material bekannt — auch in der Cochlea teilweise unspezifische Esterasen nach. Dafür spricht insbesondere die partielle Hemmung der Reaktion nach Natriumtaurocholat, welches Lipasen immer nur aktiviert, nie jedoch hemmt. Cholinesterasen konnten allerdings durch die ungehemmte Reaktion nach Ese in ausgeschlossen werden. Die partielle Hemmung nach DFP könnte den Lipaseanteil darstellen, da nach Gomori & Chessik (1953) auch Lipasen durch DFP gehemmt wer-

spalten. Die Abtrennung unspezifischer Esterasen von Lipasen erfolgt also methodisch nur teilweise vom Substrat her. Immerhin soll nach Gomori (1949) das Tween 80-Substrat (Oleinsäureester des Polymannitol, also mit ungesättigter Fettsäure) für Lipase spezifisch sein, während Tween 60 (Stearinsäureester von Polymannitol) von Esterasen und Lipasen hydrolysiert wird. Eine weitere Unterscheidung von Esterase und Lipase erfolgt durch Gallensalze, wobei Natriumtaurocholat die Lipase aktiviert, die Esterase dagegen hemmt (Barrnett & Seligman 1951). Einzelne Esterasen sollen allerdings auch durch Natriumtaurocholat aktiviert werden.

Innerhalb der unspezifischen Esterasen kann man heute histochemisch 3 Typen unterscheiden (vgl. hierzu Pearse 1961): die Esterasen A, B und C. Der Typ B wird Diisopropylfluorophosphat (DFP) in einer Konzentration von 10^{-8} M gehemmt, A und C jedoch nicht. Typ A wird ausserdem vom Natriumsalz des *p*-Hydroxymercuribenzoats (früher als *p*-Chloromercuribenzoat angesehen) gehemmt, während Typ C aktiviert wird. Die Abtrennung von Cholinesterasen einschliesslich der Acetylcholinesterase von einfachen Esterasen gelingt leicht durch DFP oder Eserin (Physostigmin), welche beide die Cholinesterasegruppe inaktivieren.

Zum Nachweis von Esterasen bedienten wir uns der Methode nach Burstone (1957). Dabei wird durch die Esterasewirkung das Naphthol AS-D acetat aufgespalten und der substituierte Naphtholrest mit einem Diazoniumsalz zu einem blauen oder rotblauen Azofarbstoff an den Stellen der Gewebsaktivität gekuppelt. Der negative Ausfall der Reaktion bei Weglassen des Substrats bzw. des Diazoniumsalzes zeigt, dass keine Niederschlagsbildung des Diazoniumsalzes bzw. keine unspezifische Bindung des Naphtholderivates vorgekommen ist. Die als positiv beschriebenen Stellen enthalten somit Esterase. Bei Zusatz von Eserin zur Inkubationslösung ändert sich das Bild nicht. Es handelt sich also bei den von uns nachgewiesenen Substanzen nicht um Pseudocholinesterase oder Acetylcholinesterase. Diese Fermente sind zwar auch in der Lage, einfache Naphtholester zu spalten, werden jedoch durch einen Zusatz von Eserin 10^{-5} M völlig gehemmt. Bei Zusatz von DFP in einer Konzentration von 10^{-4} M ergab sich nur eine geringe Abnahme der Reaktionsstärke. Auch hierdurch kann man Cholinesterasen weitgehend ausschliessen. Die massige Abnahme der Reaktionsintensität nach DFP darf wohl auf den B-Typ unspezifischer Esterasen bezogen werden, da dieser durch das organische Phosphat inaktiviert wird. Neben einer geringen Menge von B-Esterase lagen somit hauptsächlich Esterasen vom Typ A oder C vor. Nach Behandlung mit *p*-Hydroxymercuribenzoat fiel die Esterase-Reaktion eher intensiver aus. Es liegen somit neben B-Esterasen hauptsächlich C-Esterasen vor. Bei Natriumtaurocholat-Zusatz wurde die Esterase-Reaktion nur partiell gehemmt. Während der gehemmte Anteil sicher auf Esteraseaktivität zurückzuführen ist, muss es bei dem ungehemmten Anteil fraglich bleiben, wieweit Lipase oder taurocholataktivierte Esterase dafür verantwortlich ist. Da nach DFP, das die Lipasen hemmt, nur eine geringfügige Abnahme der Reaktionsstärke

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Dept of Otolaryngology
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Received October 13 1965

CONDUCTIVE RECRUITMENT

H ANDERSON and B BARR
Stockholm Sweden

From the Departments of Otolaryngology and Audiology (Heads Prof C. A Hamberger and Prof L. Holmgren) Karolin ka Sjukhuset Stockholm 60

Twenty-four cases f unilateral pure conductive loss due t fixation of the ossicular chain have been examined by bjecti e recruitment test (stapedius reflex measurement) In all of them th st pedius reflex wa recorded on acoustic stimulation of the affected ear in spite f the absence of conditions for achieving adequat stimulation owing to the conducti loss. The distan between the hearing- and reflex-thresholds diminishes with the severity of the hearing loss. Such a reduction i usuall considered to indicate recruitment. In a binaural balance test similar low-grad but definite recruitment was found That the phenomenon i dependent on the conductive defect i confirmed by comparative measurements before and after operat on. In six cases f interruption or d slocation in the ossicular chain the degree of recruitm nt wa con siderably less marked if ot entirely absent, and this applies also to a conductive loss produced xperimentally by plugging the auditory canal.

One of the most marked differences between a conductive and a sensory neural hearing loss is that the latter with extremely few exceptions, is supposed to show recruitment whereas the purely conductive hearing loss does not. As a result recruitment determinations have been ascribed great value in the differential diagnosis, and it is worth recalling that Fowler designed hi loudness balance test for the specific purpose of early diagnosis of otosclerosis.

In their classic papers Fowler (1936, 1937 1930) Steinberg & Gardner (1937) and de Bruine-Altes (1946) concluded that in cases of pure conductive loss—that is to say where the bone conduction threshold is normal—there is no recruitment Any small deviations encountered the authors tend to ascribe to irrelevant sources of error rather than to true recruitment. In the text-books on audiology the effect of a hearing loss caused by a con ductive lesion has come to be looked upon as a simple sound attenuation, such as that due to an ear plug and, as such consequently without recruit ment. When conductive impairment is accompanied by some degree of recruitment, it i usually attributed to an underlying sensory neural com ponent.

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Twenty-four cases of unilateral pure conductive loss due to fixation of the ossicular chain have been examined by objective recruitment test (stapedius reflex measurement). In all of them the stapedius reflex was recorded on acoustic stimulation of the affected ear in spite of the absence of conditions for achieving adequate stimulation owing to the conductive loss. The distance between the hearing- and reflex-thresholds diminishes with the severity of the hearing loss. Such a reduction is usually considered to indicate recruitment. In a binaural balance test a similar low-grade but definite recruitment was found. That the phenomenon is dependent on the conductive defect is confirmed by comparative measurements before and after operation. In six cases of interruption or dislocation in the ossicular chain the degree of recruitment was considerably less marked if not entirely absent, and this applies also to a conductive loss produced experimentally by plugging the auditory canal.

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inner ear Some lysosomes may be identical with the granules vacuoles, Golgi vesicles and bodies described in the supranuclear part of the vestibular sensory cells (Wersäll 1954 Smith 1956) The presence of acid phosphatase activity in the supranuclear region of the vestibular sensory epithelium points to this possibility However this supposition needs electron microscopic confirmation

It is noteworthy that most of the sites of acid phosphatase activity in the inner ear have been previously considered to have a secretory or absorptive function Structures like the stria vascularis external sulcus cells, the spiral ligament behind the external sulcus the epithelium of the limbus and the planum semilunatum have long been thought to possess a secretory function (Shambaugh 1907 and 1909 Guild 1927 Fieandt & Saxén 1937 *a* 1937 *b* Saxén 1948 and 1951 Lawrence 1956 Borghesan, 1957 Smith 1957) In view of the strong acid phosphatase activity in the Boettcher cells, these cells may also have a hitherto unsuspected secretory and/or absorptive function

The findings of present study contradict those of an earlier publication that claimed to have demonstrated acid phosphatase activity in the cochlea (Vinnikov & Titova 1957) Utilizing Gomori s lead technique Vinnikov and Titova have incubated guinea pig cochleas *in toto* From their illustrations and from the description of their observations, it is probable that these represent various artifacts In addition it should be noted that the specificity of the Gomori technique has been questioned by numerous investigators many years ago (Moog 1943 Hard & Lassek 1946 Lassek 1947 Newman Kabat & Wolf 1950)

ZUSAMMENFASSUNG

Im Innenohr embryonaler und erwachsener Meerschweinchen wurde die Aktivität der sauren Phosphatase mit der Gefrierschnitt Technik untersucht Dabei diente Naphthol AS-BI Phosphat als Substrat und Hexazonium Pararosanilin als Komplexbildner Die dunkelroten Niederschläge des Azofarbstoffes, die die Orte der Enzymaktivität anzeigen wurden in mehreren Zelltypen beobachtet In den äusseren Haarzellen beschränkte sich die Enzymaktivität auf die subcuticulare Region die bekanntlich Lysosome und Lipofuscin enthält Deshalb ist eine mögliche Beziehung zwischen saurer Phosphatase-Aktivität und einer Anhäufung unlöslicher Stoffwechsel-Endprodukte anzunehmen In den inneren Haarzellen und in den vestibulären Sinnesepithelien war die Phosphatase-Aktivität charakteristischerweise nur oberhalb des Zellkerns vorzufinden Andere Strukturen mit nennenswerter Enzymaktivität waren in der Cochlea die Stria vascularis, die äusseren Sulcuszellen und die Zellen des Limbus, weiterhin die dunklen Zellen an der Basis der Crista ampullaris. Die Ganglienzellen des Ganglion spirale und des Ganglion vestibulare enthielten ebenfalls starke bis mässige Mengen saurer Phosphatase

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inner ear *Some lysosomes may be identical with the granules, vacuoles, Golgi vesicles and bodies described in the supranuclear part of the vestibular* sensory cells (Wersäll 1954 Smith 1956) The presence of acid phosphatase activity in the supranuclear region of the vestibular sensory *epithelium points to this possibility* However this supposition needs electron microscopic confirmation

It is noteworthy that most of the sites of acid phosphatase activity in the inner ear have been previously considered to have a secretory or *absorptive function* Structures like the stria vascularis, external sulcus cells, the spiral ligament behind the external sulcus the epithelium of the limbus and the planum semilunatum have long been thought to possess a secretory function (Shambaugh 1907 and 1909 Guild 1927 Fieandt & *Saxén 1937 a 1937 b* Saxén 1948 and 1951 Lawrence 1956 Borghesan, 1957 Smith 1957) In view of the strong acid phosphatase activity in the Boettcher cells, these cells may also have a hitherto unsuspected secretory and/or absorptive function

The findings of present study contradict those of an earlier publication that claimed to have demonstrated acid phosphatase activity in the cochlea (Vinnikov & Titova 1957) Utilizing Gomori s lead technique Vinnikov and Titova have incubated guinea pig cochleas *in toto* From their illustra*tions and from the description of their observations it is* probable that these represent various artifacts In addition, it should be noted that the specificity of the Gomori technique has been questioned by numerous investigators many years ago (Moog 1943 Hard & Lassek 1946 Lassek, 1947 Newman Kabat & Wolf 1950)

ZUSAMMENFASSUNG

Im Innenohr embryonaler und erwachsener Meerschweinchen wurde die Aktivität der sauren Phosphatase *mit der Gefrierschnitt Technik untersucht* Dabei diente Naphthol AS-BI Phosphat als Substrat und Hexazonium Pararosanilin als Komplexbilder Die dunkelroten Niederschläge des Azofarbstoffes die die Orte der *Enzymaktivität anzeigen* wurden in mehreren Zelltypen beobachtet In den äusseren Haarzellen beschränkte sich die Enzymaktivität auf die subcuticulare Region die bekanntlich Lysosome und Lipofuscin enthält Deshalb ist eine mög*liche Beziehung zwischen* saurer Phosphatase-Aktivität und einer Anhäufung unlöslicher Stoffwechsel Endprodukte anzunehmen In den inneren Haarzellen und in den vestibulären Sinnesepithelien war *die Phosphatase-Aktivität charakteristischerweise* nur oberhalb des Zellkerns vorzufinden Andere Strukturen mit nennenswerter Enzymaktivität waren in der Cochlea die Stria vascularis, die äusseren Sulcuszellen und die Zellen des Limbus, *weiterhin die dunklen Zellen an der Basis der Crista ampullaris.* Die Ganglienzellen des Ganglion spirale und des Ganglion vestibulare enthielten ebenfalls starke bis mässige Mengen saurer Phosphatase

and a "negative" score) [1] It is tempting to explain at least some of these discrepancies as a result of differences between the various equipments used.

Previous Investigations

According to the original paper by Jerger *et al* (1959) normal hearers can be expected to score between 0 and 30% (generally no higher than 20%) From a more recent paper (1962 *a*) mean scores for 30 normal listeners appear to be well below 20% at all frequencies tested (250 1000 and 4000 cps)

Yantis & Decker (1964) also found mean scores to be below 20% At 4 kc, however the range of scores was found to be 0–85% 7 of the 25 Ss tested scored higher than 20% at this frequency

Hanley & Utting (1965) found a mean SISI score at 4000 cps of 42 4% (S.D. 30 75) One-third of the 48 subjects scored *60% or higher* Even for 0.5 dB increments the mean score was 5 4%

The latest published examination is by Owens (1965) who studied the effect of changing the SL at which the test is administered. The concern of this author was not the mean score nor the range of scores at different sensation levels, but only determination of the lowest presentation level at which the subjects could score 60% or higher At 20 dB SL only 1 of the 27 Ss was able to meet the 60% criterion and only at 1 frequency (4 kc) At this SL there was characteristically no response it is stated At 40 dB SL the following numbers of subjects were able to achieve a score of 60% or better 500 cps 3 Ss, 1000 cps 7 Ss and 4000 cps 4 Ss.

In the above-mentioned investigations, different types of commercial instruments were employed

For calibration, Hanley & Utting used an oscilloscope connected across the terminals of the headphone. "The voltage was recorded during that time when the pulse was not presented and gain at the moment of presentation. From these measures the change in stimulus magnitude due to the operation of the pulse was determined." In Owens study the calibration was achieved by means of sound pressure readings "During the steady state portion of the test tone at each frequency the increment dial was adjusted until a 1 dB change was observed on a sound pressure calibration unit. Jerger as well as Yantis & Decker make no mention of their method of calibration

Although some of the authors made minor departures from the original test procedure it is our impression that these modifications in test procedure cannot explain the discrepancy between test results

[1] Yantis & Decker (1964 has proposed 80% as the criterion for positive score. Owens (1965) maintains the original 60 criterion. So do Hanley & Utting (1965) but it is for 0 75 dB increment.

modulation delivered by his audiometer was a nearly trapezium shaped modulation In some other audiometers the modulation was purely sinusoidal According to Lüscher this would not merely change the numeric value of the DLI but it would also make the judgement more difficult for the patient Stressing that the normal values and their S.D. are highly dependent upon the physical qualities of the amplitude modulation, he points to the necessity of determining the normal values for each audiometer Only after testing a series of normal hearing subjects with the audiometer in question would it be possible to evaluate pathological results

Without commenting upon the possible causes for this development, we agree with Owens (1965) "By the late 1950's disappointment in the applicability of intensity difference limen tests for indicating recruitment was great enough that some clinics had abandoned them altogether

Jerger (1952) originally worked with a somewhat modified Lüscher technique, determining the DLI for modulated tones at 15 dB SL. His next step to improve the technique was a DL difference test (1953) in which the DLs determined at 10 dB and 40 dB SL were compared (a combination of a feature from the test by Denes & Naunton (1950) and the Lüscher test) Finally (Jerger *et al.*, 1959) he introduced his own test, the SISI test (SISI for Short Increment Sensitivity Index)

At the present time this test has gained considerable use both in the U.S.A and Europe different makes of SISI equipment are now available

For a complete and thorough description of the test procedure the reader is referred to the original paper but we want to recall that the signal consists of short intensity increments, superimposed at 5 second intervals, on a pure tone of constant amplitude This signal is presented at 20 dB SL. We also want to quote the description of the increments Each increment rose to maximum amplitude in 50 msec, remained at constant amplitude for 200 msec then decayed to the steady state level in 50 msec The size of each such amplitude increment was exactly 1 dB

In designing the test Jerger attached great importance to the following points (1) the stimulation was to be relatively sustained (2) the test should be simple for the tester as well as for the patient (3) the test should be as objective as possible

By interspacing 5 dB increments between the test increments measures are taken against false negative responses The possibility of false positive responses is reduced by cancellation of some of the regular increments

As the task of the tester is mainly to record the number of responses his possibility of influencing the test results is substantially reduced

It is obvious that we have a test in which the test signal is clearly defined the test procedure completely fixed, and the possibility of the tester to bias results negligible Nonetheless, some discrepancies as to the scores obtained in normal listeners have arisen (this in turn has given rise to some discussion on the criterion distinguishing between a "positive"

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FIG. 2.

The oscilloscope was used as an AC vacuum tube voltmeter. The following readings were made: (1) The voltage (*a*) across the terminals of the headphone during the steady-state tone. The attenuator of the audiometer was set at maximum output (250 cps 90 dB dial setting, 1000 cps 110 and 4000 cps 100 dB dial setting. However, when the SISI unit is connected to the audiometer the maximum output is reduced by 7.5, 8 and 9 dB for the frequencies named.) After this reading had been made the sensitivity of the instrument was increased, and the vertical position of the beam was changed to the point where only the oscillations in voltage with the increments were displayed on the screen. (2) The second reading (*b*) was the difference in voltage between *y* and *z*. From these two measurements the magnitude of the increment (*x*) was calculated in dB

$$\left(x = 20 \log \frac{\frac{1}{2}a + b}{\frac{1}{2}a} \text{ dB}\right)$$

According to the manufacturers the oscilloscope is accurate within the limits of $\pm 3\%$. The readings from the screen can be made with an accuracy of $\pm 2\%$.

With the Brüel & Kjær Level Recorder the size of the increment is directly recorded which makes the checks of calibration less time-consuming. For these measurements the audiometer was set at 60, 80 and 80 dB respectively for the frequencies employed. The accuracy of this instrument is 0.1 dB when moderate writing speeds are employed.

The use of a precision decade resistance was not practicable, as the voltage at maximum amplitude of the increment could not be kept constant during the measurement (the resistance of the LDR will change with prolonged illumination).

A large number of measurements with both these methods showed variations never exceeding ± 0.1 dB.

Subjects and Procedure

40 normal hearing subjects served as observers. They were between the ages of 17 and 38 years (mean age 27 years). The criterion of normality was negative case history and audiometric threshold — or better than 10 dB in the 125–2000 cps range, 15 dB for 4000 and 6000 cps. The subjects were mainly employees of the respective institutions and friends of

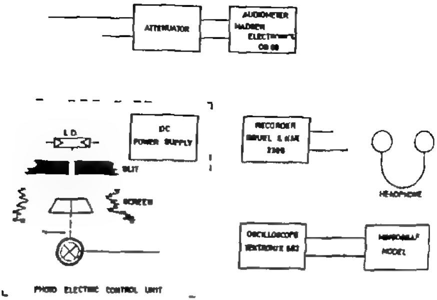

Fig. 1. Block scheme of experimental equipment.

be influenced by changes in environmental light. The voltage of the light source is stabilized against powerline voltage variations $> \pm 20\%$. The LDR is connected to the audiometer (*Madsen* OB 00) between the oscillator and the low frequency amplifier.

By experimenting with the shape of the shutter opening, we succeeded in producing variations in the output voltage of the audiometer with the desired temporal pattern. Because of the characteristics of the LDR, the actual shutter opening is not an equilateral trapezium.

During the experimentation with the shutter, it was found convenient to follow the course of the voltage variations by means of a mechanical writer (Elema-Schönander Mingograph model 81). The writing speed of this instrument is quite adequate, and the paper speed can be increased up to 50 cm/sec. In this way rise-fall time and duration can be measured accurately. Since the Mingograph is useful only for registration at low frequencies, a final control was made with an oscilloscope. This verified that the shape of the increments is constant irrespective of the carrier frequency. For periodic current control we use the scope.

The magnitude of the increments is determined by means of an external attenuator inserted between the LDR and the audiometer. In connecting the SISI unit to the audiometer, great care was taken that the connection was made in such a way that the size of the increments as measured in dB would be unaffected by audiometer attenuator position. The accuracy of the external attenuator was examined at frequent intervals by means of two different instruments, a Tektronix model 502 oscilloscope and a Brüel & Kjær Level Recorder type 2305 provided with a 10 dB potentiometer. In each instance measurements were carried out at the 3 frequencies employed with regard to all increment magnitudes used.

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TABLE 2 *Distribution of scores from 40 normal listeners at the selected test frequencies and SLs*

SISI score	10 dB SL Increment magnitude dB								20 dB SL Increment magnitude dB								40 dB SL Increment magnitude dB							
	0.5	1.0	1.5	2.0	2.5	3.0	3.5	4.0	0.5	1.0	1.5	2.0	2.5	3.0	3.5	4.0	0.5	1.0	1.5	2.0	2.5	3.0	3.5	4.0
500 cps																								
Neg. (0–20%)	40	38	35	29	12	7	3	2	40	36	21	11	4	1	0		38	4	8	3	0			
Quest. (30–50%)	0	2	5	8	7	12	6	6	0	4	15	12	7	2	1		2	14	12	2	1			
Pos. (60–100%)	0	0	0	3	11	21	31	32	0	0	4	17	29	3	39	40	0		20	35	39	40		
1000 cps																								
Neg. (0–20%)	40	37	30	16	6	3	0	0	40	38	23	8	4	2	0		40	27	13	3	0			
Quest. (30–50%)	0	3	9	11	15	6	2	1	0	2	8	14	5	2	3		0	[illegible]	8		1			
Pos. (60–100%)	0	0	1	13	19	31	38	39	0	0	9	18	31	36	37	40	0	4	19	30	39	40		
4000 cps																								
Neg. (0–20%)	40	30	17	3	2	0	0		40	29	15	3	1	0			40	4		1	0			
Quest. (30–50%)	0	7	11	15	1	1	0		0	9	11	15	1	0			0	9	13	1	0			
Pos. (60–100%)	0	3	12	22	37	39	40		0	2	14	22	38	40			0		20	38	40			

COMMENTS

The general trend of our results is a follows At low SLs scores increase with frequency At 40 dB SL they are grossly independent of frequency Consequently the increase in score with SL is most marked at low frequency

This was also the trend found by Harris (1963) in his experiments with pure tone increments in a pure tone whereas Chocholle (1955) using intensity variations of almost instantaneous onset and longer duration found the DLI to be independent of frequency even at 1 dB SL.

When comparing our results with previous investigations on the SISI test we find Our data coincide quite closely with those of Yantis & Decker both for 1 and 2 dB increments On the other hand our values are significantly lower than those obtained by Hanley & Utting This applies to the mean score for 1 dB as well as to the number of subjects with scores > 60% In these studies the test was always presented at 20 dB SL.

With regard to the number of subjects scoring 60% or higher in Owens study the agreement is only fair At 40 dB SL there seems to be a tendency for his subjects to score better at 1 kc than at 4 kc for our Ss the opposite was the case However the data were collected in different ways, and Ns are small

We can confirm Jerger's statement that scores for 1 dB increments are generally below 20% but in agreement with Yantis & Decker we find that about one in four subjects were able to score higher at 4000 cps 2 had

scores $> 60\%$. For 1.5 dB increments the number of subjects with positive scores increases to 14 and mean score increases from 16% to 40%.

Although the results might be influenced by a certain practice effect, they do imply that even minor changes of increment magnitude will cause substantial changes in SISI score.

This circumstance points to the necessity of an accurate calibration of SISI units. This in turn draws attention to the methods used for calibration. We consider the accuracy of the measurements with the oscilloscope to be sufficient. For routine checks the Brüel & Kjær level recorder should also be acceptable. In one of the previous studies the calibration was carried out by means of sound pressure readings. Due to the dynamic characteristics of sound level meters, we find such instruments unsatisfactory for measuring intensity variations of short duration. Even if the tone increment could be made constant, readings are difficult to carry out with sufficient accuracy (cf. IEC Recommendation for precision sound level meters, Geneva, 1965).

When stating that commercial SISI instrumentation appears clinically reliable Yantis & Decker make certain reservations. The calibration is important, and rise and decay times have to be approximately 50 msec. In view of our findings we want to emphasize that substantial alterations may be necessary and that in some instances calibration may be impossible because increments change with SPL and frequency.

ZUSAMMENFASSUNG

Der SISI Test ist eine wichtige Entwicklung der modernen Audiologie, besonders weil er grundsätzlich versucht, mehrere Fehler zu beseitigen, und ferner einem hohen Grad der Objektivität zustrebt. Sowohl das Testsignal als auch das Verfahren sind klar definiert, und die Möglichkeit des Untersuchers, die Ergebnisse zu beeinflussen, ist völlig reduziert. Nichtsdestoweniger sind folgende Widersprüche bei den Normalwerten aufgetaucht. Man hat das Gefühl dass technische Schwierigkeiten alle Parameter des Testsignals in Übereinstimmung mit Jergers Vorschriften zu halten teilweise hierfür verantwortlich sind. Untersuchung eines kommerziellen Geräts illustriert einige der Schwierigkeiten. Man muss besonders die Aufmerksamkeit auf die Methode der Kalibrierung richten. Ein nichtkommerzielle Ausrüstung ist beschrieben und Ergebnisse von 40 normal hörenden Personen sind gegeben. Der Test wurde bei 3 Frequenzen und bei 3 Intensitäten über der Hörschwelle ausgeführt. Acht verschiedene Grössen der kurzdauernden Amplitudenänderungen wurden verwendet.

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TABLE II *Distribution of scores from 40 normal listeners at the selected test frequencies and SL s*

	10 dB SL Increment magnitude dB								20 dB SL Increment magnitude dB								40 dB SL Increment magnitude dB							
SISI score	0.5	1.0	1.5	2.0	2.5	3.0	3.5	4.0	0.5	1.0	1.5	2.0	2.5	3.0	3.5	4.0	0.5	1.0	1.5	2.0	2.5	3.0	3.5	4.0
250 cps																								
Neg (0– 20%)	40	38	35	29	12	7	3	2	40	36	21	11	4	1	0		38	21	8	3	0			
Quest (30– 50%)	0	2	5	8	7	12	6	6	0	4	15	[illegible]	7	2	1		2	11	12	2	1			
Pos. (60–100%)	0	0	0	3	11	21	31	32	0	0	4	17	29	37	39	40	0	2	20	35	39	40		
1000 cps																								
Neg. (0– 20%)	40	37	30	16	6	3	0	0	40	38	23	8	4	2	0		40	27	13	3	0			
Quest (30– 50%)	0	3	9	11	15	6	2	1	0	2	8	14	5	2	3		0	9	8	7	1			
Pos (60–100%)	0	0	1	13	19	31	38	39	0	0	9	18	31	36	37	40	0	4	19	30	39	40		
4000 cps																								
Neg. (0– 20%)	40	30	17	3	2	0	0		40	29	15	3	1	0			40	21	7	1	0			
Quest (30– 50%)	0	7	11	15	1	1	0		0	0	11	15	1	0			0	0	13	1	0			
Pos. (60–100%)	0	3	12	22	37	39	40		0	2	14	22	38	40			0	7	20	38	40			

COMMENTS

The general trend of our results is a follows At low SL s scores increase with frequency At 40 dB SL they are grossly independent of frequency Consequently the increase in score with SL is most marked at low frequency

This was also the trend found by Harris (1963) in his experiments with pure tone increments in a pure tone whereas Chocholle (1955) using intensity variations of almost instantaneous onset and longer duration found the DLI to be independent of frequency even at 1 dB SL.

When comparing our results with previous investigations on the SISI test we find Our data coincide quite closely with those of Yantis & Decker both for 1 and 2 dB increments On the other hand our values are significantly lower than those obtained by Hanley & Utting This applies to the mean score for 1 dB as well as to the number of subjects with scores ≥60% In these studies the test was always presented at 20 dB SL

With regard to the number of subjects scoring 60% or higher in Owens study the agreement is only fair At 40 dB SL there seems to be a tendency for his subjects to score better at 1 kc than at 4 kc, for our Ss the opposite was the case However the data were collected in different ways, and Ns are small

We can confirm Jerger s statement that scores for 1 dB increments are generally below 20% but in agreement with Yantis & Decker we find that about one in four subjects were able to score higher at 4000 cps II had

scores > 60 %. For 1.5 dB increments the number of subjects with positive scores increases to 14 and mean score increases from 16 % to 40 %.

Although the results might be influenced by a certain practice effect, they do imply that even minor changes of increment magnitude will cause substantial changes in SISI score.

This circumstance points to the necessity of an accurate calibration of SISI units. This in turn draws attention to the methods used for calibration. We consider the accuracy of the measurements with the oscilloscope to be sufficient. For routine checks the Brüel & Kjær level recorder should also be acceptable. In one of the previous studies the calibration was carried out by means of sound pressure readings. Due to the dynamic characteristics of sound level meters, we find such instruments unsatisfactory for measuring intensity variations of short duration. Even if the tone increment could be made constant, readings are difficult to carry out with sufficient accuracy (cf. IEC Recommendation for precision sound level meters, Geneva, 1965).

When stating that commercial SISI instrumentation appears clinically reliable, Yantis & Decker make certain reservations. The calibration is important, and rise and decay times have to be approximately 50 msec. In view of our findings we want to emphasize that substantial alterations may be necessary, and that in some instances calibration may be impossible because increments change with SPL and frequency.

ZUSAMMENFASSUNG

Der SISI-Test ist eine wichtige Entwicklung der modernen Audiologie, besonders weil er grundsätzlich [illegible], mehrere Fehler zu beseitigen, und ferner einen hohen Grad der Objektivität anstrebt. Sowohl das Testsignal als auch das Verfahren sind klar definiert, und die Möglichkeit des Untersuchers, die Ergebnisse zu beeinflussen, ist völlig reduziert. Nichtsdestoweniger sind einige Widersprüche bei den Normalwerten aufgetaucht. Man hat das Gefühl, dass technische Schwierigkeiten, alle Parameter des Testsignals in Übereinstimmung mit Jergers Vorschriften zu halten, teilweise hierfür verantwortlich sind. Untersuchung eines kommerziellen Geräts illustriert einige der Schwierigkeiten. Man muss besonders die Aufmerksamkeit auf die Methode der Kalibrierung richten. Eine nicht kommerzielle Ausrüstung ist beschrieben, und Ergebnisse von 40 normal hörenden Personen sind gegeben. Der Test wurde bei 3 Frequenzen und bei 3 Intensitäten über der Hörschwelle ausgeführt. Acht verschiedene Grössen der kurzdauernden Amplitudenänderungen wurden verwendet.

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Bentzen, O. 1953. Investigations [illegible] short tones. *Thesis*, Universitetsforlaget, Aarhus.

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TABLE 2 *Distribution of scores from 40 normal listeners at the selected test frequencies and SL s*

	10 dB SL Increment magnitude dB								20 dB SL Increment magnitude dB								40 dB SL Increment magnitude dB							
SISI score	0.5	1 0	1.5	2.0	2.5	3 0	3.5	4 0	0.5	1 0	1.5	2 0	2.5	3 0	3 5	4 0	0.5	1 0	1.5	2.0	2.5	3 0	3.5	4 0
250 cps																								
Neg. (0– 20%)	40	38	35	20	12	7	3	2	40	30	21	11	4	1	0		38	21	8	3	0			
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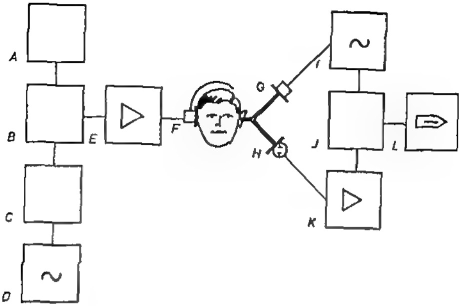


Fig 1 Test set up: *A* audi meter (Amplivox); *B* mixing pad *C* witch; *D* oscillator (Brüel & Kjær type 1022) *E* amplifier *F* earpho e for stimuli t nes *G* t lephone f r test t ne *H* condenser microphone *I* oscillat r (frequency 520 Hz) *J* pl se and amplitud control for counterbalancing; *K* amplifier and filter (1/3 octave 500 Hz) *L* level recorder (Brüel & Kjær type 2305)

oscillator and the mixing pad B The symbols G–I stand for the electro-acoustic bridge, with a counterbalancing device to obtain a high degree of sensitivity in principle identical with the apparatus of Terkildsen & Scott Nielsen (1960)

Measurements

The measurements were performed on two normal hearing subjects a 30 year-old female and a 28 year-old male The reflex threshold as function of frequency was registered in the frequency range 250–2000 Hz Both subjects had reflex thresholds within normal values After counterbalancing the electro-acoustic bridge the primary tone is introduced 10 dB above reflex threshold In the experiments 1–3 the primary tone frequency was set to 1000 Hz, in the fourth experiment several different primary frequencies were arbitrarily chosen When the muscle contraction reaches the stationary state the second tone is superimposed

Experiment 1

The level of the second tone was set to 10 dB above reflex threshold Frequencies of the second tone were 250 500 750 900 950 1025 1050 1100 1500 and 2000 Hz. A marked reflex reactivation response was obtained to all secondary tones referred to A typical example of the impedance shift is shown in Fig 2 *a*

Experiment 2

This experiment was intended to decide if the reactivation reflex threshold differed from the ordinary reflex threshold in the frequency range on

FIG. 2. Recordings of impedance change See text.

both sides of the primary tone The second tone is presented intermittently at different levels. Frequencies of the second tone were 700 900 1100 and 1300 Hz. The reactivation reflex threshold was found to equal the values of the ordinary reflex threshold, within an accuracy of 1–2 dB

Experiment 3

The results of experiments 1 and 2 seem to show that the phenomenon of reactivation does not include any "critical bandwidth" Lüscher (1930) in his experiments was not able to observe any contraction of the stapedius muscle by adding an identical tone It is reasonable, however to question if his observation describes a general condition In order to clarify this, we performed the following two tests

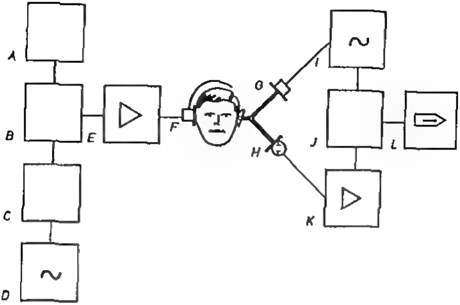
In the first test the secondary tone was set to the same level as the continuous primary tone and at a frequency differing only about 0.5 Hz from the frequency of the primary tone. The subject perceived beats in the stimulus ear and corresponding impedance shifts were registered on the contralateral ear as shown in Fig 2 *b*

These results indicate that no critical bandwidth exists between the primary and secondary tone, but give no definite answer to the question as to what will happen when an identical tone is superimposed This may be achieved quite simply by raising the sound pressure level of the primary tone by 3 dB As shown in Fig 2 *c* the increase of the tone produces a marked impedance shift.

Experiment 4

In the former experiments (1–3) the frequency of the primary tone was 1000 Hz. In order to investigate the results for other primary frequencies the following tests were performed

( ) The procedure in experiment 1 was repeated with a primary frequency of 2000 Hz and with secondary frequencies of 1000 1500 1800 1950 2050 and 2200 Hz. In the presence of a primary tone of 2000 Hz the secondary tones referred to produced marked reflex reactivations.



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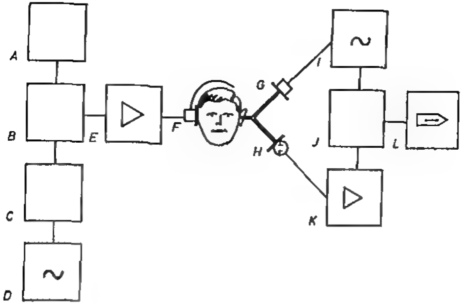

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Experiment 1

The level of the second tone was set to 10 dB above reflex threshold. Frequencies of the second tone were 250, 500, 750, 900, 950, 1025, 1050, 1100, 1500 and 2000 Hz. A marked reflex reactivation response was obtained to all secondary tones referred to. A typical example of the impedance shift is shown in Fig. 2 *a*.

Experiment 2

This experiment was intended to decide if the reactivation reflex threshold differed from the ordinary reflex threshold in the frequency range on

TABLE 3 *Acoustic and vestibular manifestations in H.S.C. disease*

	No. of cases		
	Unilateral	Bilateral	Total
Deafness of			
unknown type	9	13	22
perceptive type	1	7	8
conduction type	5	[illegible]	6
Vestibular manifestations	15	1	[illegible]
Acoustic and vestibular manifestations	11	6	17
Total	41	37	[illegible]

Apart from these cases, otitis externa has often been described in the presence of major destructions of the temporal bone close to the auditory meatus, but without polyp or fistula.

Acoustic and Vestibular Changes in H.S.C. Disease

Since 45% of the patients having destruction of the temporal bone were under 3 years of age, and since several of the adult patients have not had acoustic or vestibular tests, the figures listed in Table 3 must be interpreted as minimum values.

In 17 cases with hearing impairment of *unknown type* without vestibular changes, there was a corresponding destruction of the temporal bone. In the remaining 5 cases there were no defects of the temporal bone and no otitis or neurological changes.

Hearing impairment of the *perceptive type* without other acoustic vestibular changes was usually fairly severe and accompanied by corresponding destruction of the petrous portion. Three patients, however, showed no radiological signs of destruction in the temporal bones and no signs of neurological loss. The cause of the hearing impairment in these 3 cases may possibly have been granulomas affecting the intracranial course of the acoustic nerve. Hearing impairment of the conduction type is due to granulomas in the middle ear.

As regards vestibular manifestations, *spontaneous nystagmus* without acoustic findings, was present in 6 cases. Four of these patients also had cerebellar and bulbar symptoms, and the nystagmus was due to changes in the brain stem. In the remaining 2 cases the nystagmus was due to destruction around the internal porus acusticus.

Isolated reduction of vestibular function has only been reported in one case. In this case there was no destruction of the temporal bone and no neurological abnormalities (Wallace, 1949).

Vertigo without objective acoustic vestibular findings has been reported

changes The majority of the operated patients had granulomatous masses in the middle ear and epithympanon, while in some cases no masses were present (Heath 1931 Rowland 1928)

The aural discharge in this group appears to be caused by the close relation of the specific lesions to the middle ear Increased intratympanic pressure from granulations or secretory products of specific changes of the middle-ear mucosa may possibly lead to perforation of the drum

Group 3 Aural discharge polyp or granulation tissue in the auditory meatus and destruction of the temporal bone The polyp has always been rather large, arising in the majority of cases from the meatal wall in a few cases from the middle ear through the pars flaccida or pars tensa Perforation of the meatal wall by granulomatous masses may happen in all sites, but as a rule posteriorly or superiorly close to the drum The polyp grows quite fast and recurs in a short time After removal of the polyp the aural discharge often ceases, unlike the discharge arising in the middle ear which is primarily chronic as already mentioned

Microscopic examination of the polyps has in a few cases led to the diagnosis of H S.C. disease but sometimes it has shown only non specific granulation tissue

The aural discharge in this group is usually due to a polyp arising from the meatus in the presence of an intact drum Granulomatous masses in the temporal bone erode the meatal walls, form a fistula in the bone and spread out through the meatal skin This gives rise to a local reaction of the skin, delimited otitis externa with exudation

Group 4 Aural discharge without destruction of the temporal bone and without meatal changes has been reported in 21 cases (4 2%) including 13 with bilateral involvement The aural discharge arising from the middle ear was primarily chronic spontaneous and not accompanied by an elevation of temperature or pain which militates against simple otitis media These patients showed no tumour formation behind the ear

Seventeen of these 21 patients had manifestations in the skin, lymph nodes mucous membranes, or viscera It is reasonable to assume therefore, that these patients may also have involvement of the middle ear mucosa and the mucosa of the Eustachian tube in the form of reticulo-endothelial hyperplasia

Otitis Externa

Otitis externa has been found in 14 cases (2.8) 9 of which were bilateral as a rule in the form of reddening or swelling of the skin with epithelial desquamation Most of these patients had exanthema of the trunk and a few had papules and crusts, like those on the trunk in the auditory meatus.

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As regards vestibular manifestations, *spontaneous nystagmus* without acoustic findings, was present in 6 cases. Four of these patients also had cerebellar and bulbar symptoms, and the nystagmus was due to changes in the brain stem. In the remaining 2 cases the nystagmus was due to destruction around the internal porus acusticus.

Isolated reduction of vestibular function has only been reported in one case. In this case there was no destruction of the temporal bone and no neurological abnormalities (Wallace 1940).

Vertigo without objective acoustic vestibular findings has been reported

changes The majority of the operated patients had granulomatous masses in the middle ear and epithympanon while in some cases no masses were present (Heath 1931 Rowland, 1928)

The aural discharge in this group appears to be caused by the close relation of the specific lesions to the middle ear Increased intratympanic pressure from granulations or secretory products of specific changes of the middle ear mucosa may possibly lead to perforation of the drum

Group 3 Aural discharge polyp or granulation tissue in the auditory meatus and destruction of the temporal bone The polyp has always been rather large, arising in the majority of cases from the meatal wall in a few cases from the middle ear through the pars flaccida or pars tensa Perforation of the meatal wall by granulomatous masses may happen in all sites but as a rule posteriorly or superiorly close to the drum The polyp grows quite fast and recurs in a short time After removal of the polyp the aural discharge often ceases, unlike the discharge arising in the middle ear which is primarily chronic as already mentioned

Microscopic examination of the polyps has in a few cases led to the diagnosis of H S C. disease but sometimes it has shown only non specific granulation tissue

The aural discharge in this group is usually due to a polyp arising from the meatus in the presence of an intact drum Granulomatous masses in the temporal bone erode the meatal walls, form a fistula in the bone and spread out through the meatal skin This gives rise to a local reaction of the skin delimited otitis externa with exudation

Group 4 Aural discharge without destruction of the temporal bone and without meatal changes has been reported in 21 cases (4.2%) including 13 with bilateral involvement The aural discharge arising from the middle ear was primarily chronic, spontaneous and not accompanied by an elevation of temperature or pain which militates against simple otitis media These patients showed no tumour formation behind the ear

Seventeen of these 21 patients had manifestations in the skin, lymph nodes, mucous membranes, or viscera It is reasonable to assume therefore that these patients may also have involvement of the middle ear mucosa and the mucosa of the Eustachian tube in the form of reticulo-endothelial hyperplasia

Otitis Externa

Otitis externa has been found in 14 cases (2 8) 9 of which were bilateral, as a rule in the form of reddening or swelling of the skin with epithelial desquamation Most of these patients had exanthema of the trunk and a few had papules and crusts, like those on the trunk in the auditory meatus.

TABLE 3 *Acoustic and vestibular manifestations in H.S.C. disease*

	No. of cases		
	Unilateral	Bilateral	Total
Deafness of			
unknown type	9	13	22
perceptive type	1	7	8
conduction type	5	0	5
Vestibular manifestations	15	1	16
Acoustic and vestibular manifestations	11	6	17
Total	41	27	68

Apart from these cases, otitis externa has often been described in the presence of major destructions of the temporal bone close to the auditory meatus, but without polyp or fistula.

Acoustic and Vestibular Changes in H.S.C. Disease

Since 45% of the patients having destruction of the temporal bone were under 3 years of age, and since several of the adult patients have not had acoustic or vestibular tests, the figures listed in Table 3 must be interpreted as minimum values.

In 1 cases with hearing impairment of *unknown type* without vestibular changes, there was a corresponding destruction of the temporal bone. In the remaining 5 cases there were no defects of the temporal bone and no otitis or neurological changes.

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These changes usually appear at an early stage of the disease and were in 14 cases the initial signs of H.S.C. disease.

As a rule there was swelling and reddening of the mucous membrane, especially on the gingivae usually with small or larger ulcerations having yellowish margins, and central necrosis. There will be pronounced alveolar pyorrhoea and usually loss of alveolar septa, loose teeth, and destructions of the upper and lower jaw. The course is prolonged, painful, with frequent recurrences. Histologically the ulcers are made up of reticulo-endothelial cells. In a few instances, ulcers have been observed on the mucosa of the soft and hard palate (Karlén 1952)

Hyperplastic pharyngitis has been described in a number of cases. In one case (Turner Davidson & White, 1925) there were small yellowish nodules in the pharyngeal epiglottic, and laryngeal mucosa.

Chronic rhinitis and rhinopharyngitis have also been reported. No microscopic study of the nasal or pharyngeal mucosa has been done

Larynx Trachea and Bronchi

Granulomat us changes of the larynx, trachea, and bronchi have been found in 7 cases (1 4 %) manifesting themselves as multiple greyish-yellow tumours, scattered diffusely in the mucosa or as pronounced diffuse thickening of the mucosa (Turner Davidson & White, 1925) or as deep ulcers (Müller 1938)

Treatment and Prognosis

X ray therapy in small or moderate doses is at present generally acknowledged as the best ymptomatic treatment. In many cases the aural discharge has decreased or ceased, the polyp or swelling has diminished and the progression of the destruction has been arrested. In most other cases the treatment has not improved the acoustic and vestibular manifestations, but there have been exceptions (Chester & Kugel 1932 Jones, 1939)

Cortisone a d ACTH have occasionally hown a favourable and rapid effect, also upon the aural discharge (Bass, Sapin & Hodes, 1953) but the effect ha been temporary

Antibi tics may *exert a good effect upon the aural discharge* in the presence of secondary infecti n but antibiotics alone cannot stop it. A combination of X rays and antibi tics is to-day the best method for treating th E.N T manifestation of H S.C disease with secondary infection. Surgery alone is of no essential therapeutic effect but is of diagnostic aid

In 51 cases resection of the m stoid process has been carried out, bilaterally in 17. The operative wound howed very little tendency to healing, and in 33 cases (on both sides in 11) a chronic fistula developed in the w und on th mastoid process. The fistulae were resistant to local

ethmoid cells Operation showed the sinuses to be filled with yellowish granulomatous masses surrounded by bone destruction

Ethmoid and Sphenoid Cells

Destruction and filling of the ethmoid cells has been reported in only 11 cases (2 2%) and of the sphenoid cells in 7 (1 4%) but attention was seldom directed at these cavities The orbital bones and sphenoid bone are often involved and the granulomatous masses from these sites may easily invade th ethmoid or sphenoid cells It must be presumed therefore that these regions are in fact involved considerably more often than indicated by the reported values

Nose

Destruction of the nasal bones and granulomatous tumours in the nasal cavity have been reported in 6 cases (1.2%) including 2 in which this was the initial sign

As a rule, the lateral nasal wall is destroyed and this is followed by granulomatous invasion of the maxillary antrum The granulomas may be situated primarily in the nasal bones or they may have spread thence from the surroundings

Tonsils

Pronounced tonsillar hypertrophy has been reported in 31 cases (6 2%) This is due to hyperplasia of reticulo-endothelial cells, which have frequently been demonstrated histologically The tonsillar hypertrophy usually accompanied by diffuse lymph node enlargement may be monstrous and may occasionally in a short time lead to obstruction of the fauces (Mikulowski 1957)

Tonsillitis has been recorded in 24 cases (4 8%) in the great majority of cases ulcerative with several small or a few larger ulcers on the surface of the tonsil Histologically the ulcers have been built up of reticulo-endothelial cells in the margins with central necrosis (Ighenti 1931 Letterer 1933) In these cases too the tonsils have been hypertrophic The cases of tonsillitis too have usually been accompanied by diffuse enlargement of the lymph nodes

Thus, a total of 55 cases (11 0%) have exhibited specific changes of the tonsils, but it must be presumed that the tonsils have been affected in further cases, as diffuse hyperplasia of the reticulo-endothelial system as a rule involves the tonsils at an early stage

Oral Nasal and Pharyngeal Mucosa

Changes of the oral mucosa have been reported in 125 cases (25%) manifesting themselves as ulcerative gingivitis and ulcerative stomatitis

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and antibiotic therapy and in several cases it could not be closed not even by X ray therapy The risk of operative damage to the facial nerve is considerable because of the completely imperspicuous approach and indeed 8 cases had postoperative facial palsy

The course of the disease is usually chronic, in some cases sub-chronic, exacerbations alternating in a typical way with remissions Old foci heal spontaneously but new destructions appear If the patient survives for a sufficient length of time without the process coming to a stop hardly any sign will be missing The prognosis is doubtful in all cases It depends upon the site of the granulations, and it is the more favourable the older the patient is and the earlier X ray therapy is instituted

ZUSAMMENFASSUNG

Auf Grund der Studien von 500 in der Literatur berichteten Fällen wird über ONH Manifestationen bei Hand Schüller-Christianscher Krankheit berichtet Von den früher publizierten Fällen der Krankheit hatten 90% der Fälle eine oder mehrere ONH Manifestationen besonders chronischen Ohrenfluss, Destruktion des Schläfenbeines akustische und vestibuläre Symptome periphäre Fazialislähmung sowie Granulome in der Nase und Nasenhöhlen Ausserdem wurden spezifische Tonsillitis mit Tonsilhypertrophie ulzeröse Stomatitis und in einigen Fällen auch spezifische Änderungen der Schleimhaut im Larynx Trachea und Bronchien beschrieben Häufigkeit und Natur der Symptome werden beschrieben

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C-REACTIVE PROTEIN AND OPERATION

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The occurrence of C-reacti e protein (CRP) wa studied after 167 otolary gological operati ns. CRP ppeared in blood serum of patients in 113 cases out of 167 In the case of tonsillectomies the incidence of positive test for CRP was th highest 47 out of 51 Tonsillectomies and or adenoidectomies d ne under general anesthesia showed a lower frequency of positive CRP tests than tonsillectomies under local anesthesia. In the series studied, there were no postoperati e complicati s, and therefore other points have to be taken into consideration when assessing the reason why CRP did not ppea in co nection with all operation f the same kind.

In a previous paper Tarkkanen & Tuomioja (1966) studied the presence of C-reacti e protein (CRP) in otolaryngological diseases. The test for CRP was positive in 117 cases out of 819 Acute peritonsillitis showed the highest incidence of positive tests, 93 per cent, and maxillary carcinoma with 90 per cent, followed next. In chronic suppurative otitis media CRP appeared in only 2 per cent.

The p esent investigation was prompted by the interesting aspects presented by CRP after surgical procedures Baldauf & Jacoby's report (1959) is th only one earlier published on CRP in connection with operations and postoperati e complications. They had 33 patients and each of them howed CRP in blood serum following a surgical or neurosurgical operation. The highest titres were found during the first few postoperative days (1–4 days) Postoperative complications caused elevated titres for prolonged periods. CRP disappeared from the blood in 7–11 days if there were no complication

MATERIAL AND METHODS

The material consisted of 167 patients operated on at the Helsinki University Otolaryngological Hospital. CRP was determined from two samples, taken immediat ly before and 24 hours after operation. Only patients with a negative preoperative test for CRP were accepted The operations were performed under local or general anesthesia The local anesthetic used w 0.5–1 per cent Carbocain® with adrenalin The

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TABLE 2 *C-reactive protein after tonsillectomies and/or adenoidectomies which are classified by the anesthetic agents*

Operation	Anesthetic agent	No. of cases	Test for CRP Positive	Negative
Tonsillectomy	Carbocain® with adrenalin	44	42	2
	Ethydan® & Fluothane®	4	4	—
	Ethydan®	2	—	2
	Fluothane®	1	1	—
Tonsillectomy and adenoidectomy	Ethydan® & Fluothane®	10	7	3
	Ethydan®	1	1	—
	Fluothane®	3	2	1
Adenoidectomy	Ethydan® & Fluothane®	6	3	3
	Ethydan®	2	—	2
	Fluothane®	4	2	2

used (Table 2). Patients who had their operations done under general anesthesia were from 2 to 16 years of age. Tonsillectomies were performed under local anesthesia on patients aged between 17–64 years.

Patients subjected to tonsillectomy under local anesthesia showed a significantly higher incidence of CRP than those under general anesthesia. The other groups are too small to allow conclusions as regards either Ethydan® or Fluothane®.

DISCUSSION

According to the literature CRP is supposed to be demonstrable in blood serum within 24 hours in acute infectious diseases or in conditions in which tissue destruction takes place, e.g. cardiac infarction (Keitel, Diesner & Bannert, 1964). The results of CRP determinations in this study differ from those of Baldauf and Jacoby. CRP did not appear in all cases of similar operations, e.g. in a total of 20 mastoidectomies performed under local anesthesia, CRP appeared in 12 cases. In the case of stapes operations, associated with far less soft tissue surgery, CRP was demonstrable in only two cases out of 10. The type of anesthesia and the age of the patient may bear some relationship to the incidence of CRP after tonsillectomies and/or adenoidectomies: the highest incidence of CRP was encountered in adults anesthetized locally for tonsillectomy.

ZUSAMMENFASSUNG

Die Verf asser haben in einem anderen Artik el d. Vorkommen des C-reaktiven Prot ins be i lary ngologischen Krankheiten untersucht; dabei wurd das C-RP bei 117 on insgesamt 819 Fällen vorgefunden. N ch allgemeinchirurgischen und

TABLE 1. *Tests for CRP 24 hours after an otolaryngological operation. 167 cases and operations*

Operation	No. of cases	Test for CRP: Positive	Test for CRP: Negative
Mastoidectomy	20	12	8
Stapes operation	10	2	8
Myringoplasty	5	2	3
Decompression of the facial nerve	2	2	
Plastic surgery for the ears	6	1	5
Operation for deviated septum	11	8	3
Ethmoidectomy	4	2	2
Dolomite implantation in ozaena	3	2	1
Reduction of nasal fracture	3	2	1
Rhinoplasty	3	3	
Tonsillectomy	51	47	4
Adenoidectomy	12	5	7
Tonsillectomy and adenoidectomy	14	10	4
Laryngectomy	2	2	
Extirpation of malignant tumors in skin	3	3	
Extirpation of benign tumors in skin	11	5	6
Mediastinoscopy	2	2	
Other endoscopies	2		2
Extirpation of glomus caroticum	3	3	
Total	167	113	54

anesthetic agents for general anesthesia were Ethydan® and/or Fluothane®.

The CRP determinations were done at the State Serum Institute using the APC test (Tuomioja & Kajanne 1956, Tuomioja *et al.* 1966, Salo & Tuomioja, 1968).

RESULTS

Table 1 shows the results of CRP determinations 24 hours after the operations. Each patient had only one operation done and a negative test for CRP immediately before operation.

As evident from Table 1, CRP appeared in blood serum in 2/3 of all cases, but it did not appear in all cases of similar operations, for instance after mastoidectomies for chronic suppurative otitis media CRP occurred in 12 cases out of 20. Tonsillectomies showed the highest incidence of CRP, 47 out of 51 cases. After adenoidectomies negative tests for CRP outnumbered the positive tests.

Because the type of anesthesia may have some influence on the occurrence of CRP, the tonsillectomies were classified by the anesthetic agent

TABLE 2. *C-reactive protein after tonsillectomies and/or adenoidectomies which are classified by the anesthetic agents*

Operation	Anesthetic agent	No. of cases	Test for CRP	
			Positive	Negative
Tonsillectomy	Carbocain® with adrenalin	44	42	2
	Ethydan® & Fluothane®	4	4	—
	Ethydan®	2	—	2
	Fluothane®	1	1	—
Tonsillectomy and adenoidectomy	Ethydan® & Fluothane®	10	7	3
	Ethydan®	1	1	—
	Fluothane®	3	2	1
Adenoidectomy	Ethydan® & Fluothane®	6	3	3
	Ethydan®	2	—	2
	Fluothane®	4	2	2

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According to the literature CRP is supposed to be demonstrable in blood serum within 24 hours in acute infectious diseases or in conditions in which tissue destruction takes place, e.g. cardiac infarction (Keitel, Diesner & Bannert, 1964). The results of CRP determinations in this study differ from those of Baldauf and Jacoby. CRP did not appear in all cases of similar operations, e.g. in a total of 20 mastoidectomies performed under local anesthesia, CRP appeared in 12 cases. In the case of stapes operations, associated with far less soft tissue surgery, CRP was demonstrable in only two cases out of 10. The type of anesthesia and the age of the patient may bear some relationship to the incidence of CRP after tonsillectomies and/or adenoidectomies; the highest incidence of CRP was encountered in adults anesthetized locally for tonsillectomy.

ZUSAMMENFASSUNG

Die Verfasser haben in einem anderen Artikel das Vorkommen des C-reaktiven Proteins bei otolaryngologischen Krankheiten untersucht; dabei wurde das C-RP bei 117 von insgesamt 819 Fällen vorgefunden. Nach allgemeinchirurgischen und

neurochirurgischen Operationen ist C-RP gut eine Woche im Serum des Patienten vorgefunden worden Bei otolaryngologischen Operationen gibt es in dieser Hinsicht keine Berichte in der Literatur Die Verfasser studierten das postoperative Auftreten von C-RP bei 167 Patienten In das Untersuchungsmaterial wurden nur Patienten die preoperativ einen negativen C-RP Befund hatten eingereiht C-RP wurde bei / der Fälle vorgefunden Die höchste Frequenz trat nach Tonsillektomie auf d h 48 Fälle von 51 zeigten einen positiven C-RP Befund Tonsillektomien unter örtlicher Betäubung wiesen in statistisch signifikantem Masse öfter eine C-RP Positivität als die unter Narkose ausgeführten Tonsillektomien und/oder Adenotomien auf Das Alter hat möglicherweise gewisse Bedeutung da die örtlichbetäubten Patienten alle erwachsen waren während letztere Gruppe nur aus Kindern bestand Zusätzliche Untersuchungen sind jedoch nötig, um den eventuellen Anteil der Betäubungs- und Narkosemittel bei postoperativer C-RP Positivität ermitteln zu können

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C-REACTIVE PROTEIN IN OTOLARYNGOLOGICAL DISEASES

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C-reactive protein (CRP) was determined in 819 patients suffering from various otolaryngological diseases. The test for CRP was positive in 117 cases and negative in 702. The highest frequency of positive tests, 93 per cent, was obtained in acute peritonsillitis. The results in this study support earlier reports in general chronic suppurative otitis media with or without cholesteatoma showed a surprisingly low incidence of positive tests, 2 per cent

Before the advent of biochemotherapy pneumococcal pneumonia had a grave prognosis and a great deal of attention was therefore paid to the bacteriology and serology of this disease In a review Keitel Diesner & Bannert (1964) describe some results of this work in the following terms

In differentiating antibodies against various strains of pneumococci, a carbohydrate was discovered in the cell body of pneumococci Because it differed both chemically and immunologically from polysaccharide A of the capsule, and from nucleoprotein B, it was called the C substance Tillet & Francis (1930) found that at the acute phase of the disease the serum of patients suffering from pneumonia gave a precipitin reaction with this C substance hence the name of this precipitin in the serum, C-reactive protein (CRP) It is still a controversial question whether this protein belongs to the albumins or globulins. The origin and significance of CRP are still not definitely known in spite of the great number of studies carried out on CRP In rabbits, a protein C_xRP appears in blood serum after skin lesions and radiation. Local ischemia or tissue destruction seems to be a prerequisite for the appearance of CRP which occurs in several other diseases (excluding pneumonia) e.g various inflammatory diseases, rheumatic fever cardiac infarction, and malignant neoplasms. In all probability it is a question of decomposition product of cell proteins. CRP is usually demonstrable in blood serum within 24 hours in acute inflammatory conditions and disappears in a few days during convalescence.

There are few reports on CRP in ear nose and throat diseases. Carlens (1941) studied 100 cases of acute otitis media for CRP and found it to be present in 54 Marino (1959) assessed the changes in CRP after electrical stimulation of the tonsils According to him, a negative test for CRP excludes focal tonsillar infection as a cause of distant pathological manifestations. After electrical stimulation of the tonsils, the test for

TABLE 1 *C reactive protein (CRP) in otolaryngological diseases 819 cases*

Disease	No of cases	Test for CRP Positive	Negative
Chronic suppurative otitis media	112	2	110
Chronic suppurative otitis media with cholesteatoma	56	1	[illegible]
Acute mastoiditis	11	8	3
Otosclerosis	1	1	0
Microtia	14	—	14
Protruding ears	11	—	11
Ménière's disease	16	—	16
Acute pansinusitis	[illegible]	4	16
Deviated nasal septum	51	1	50
Ozaena	14	—	14
Epistaxis	6	2	4
Nasal fracture	4	2	2
Dacryocystitis	27	1	26
Chronic maxillary sinusitis	38	4	34
Chronic ethmoiditis	18	3	15
Chronic frontal sinusitis	3	—	3
Acute peritonsillitis	[illegible]	60	1
Chronic tonsillitis	253	15	238
Carcinoma of the maxilla	10	9	1
Carcinoma of the larynx	21	10	11
Carcinoma of the hypopharynx	6	4	2
Total	819	11[illegible]	702

CRP was *positive in chronic tonsillitis in eight cases out of 30 and in all* 18 cases of acute tonsillitis. Keitel, Diesner & Bannert (1964) prepared a review paper on CRP. *Their own material consisted of 15[illegible]8 cases,* including 48 of otolaryngological origin. The purpose of this paper is to study the occurrence of CRP in ear, nose and throat diseases on the basis of a larger series than hitherto reported on.

MATERIAL AND METHODS

The material consisted of 819 unselected patients seen in the Outpatient Department of the Helsinki University Otolaryngological Hospital.

The CRP *determinations* were carried out at the State Serum Institute using the APC test (Tuomioja & Kajanne 1956; Tuomioja *et al.* 1956; Salo & Tuomioja, 1958).

RESULTS

The results of CRP determinations in various ear, nose and throat diseases are given in Table 1.

As seen above the test for CRP was positive in chronic suppurative otitis media in only three cases out of 168, whereas CRP appeared in blood serum in eight cases out of 11 in acute otitis media. Comparatively the largest group of positive tests for CRP occurred in acute peritonsillitis, viz. 50 out of 54 (93 per cent) Of the malignant neoplasms, carcinoma of the maxilla showed CRP in 90 per cent and carcinoma of the larynx in 42 per cent. The highest titres in CRP determinations were recorded in acute bacterial infections like peritonsillitis and mastoiditis, in both of which they were mainly between 1 4–1 32 In chronic tonsillitis the titres ranged between 1 1–1 4

DISCUSSION

This material includes many diseases in which CRP cannot be expected t occur e.g. microtia and Menière s disease. Thus the incidence of tests positive for CRI is fairly low 14 per cent. Because the presence of CRP i associated with the acute phase of infection the low incidence of CRP in chronic suppurative otitis media (2 per cent) is more readily under tandable In chronic suppurative otiti media, especially when combined with cholesteatoma, there is always bone necrosis, and so a higher incidence f positive t ts f r CRP was to be expected Acute pansinusitis seems to have been severe in only 20 per cent to judge from the low in idence of CRP Maxillary c rcinoma stands in sharp contrast to this disease th incidence of CRP was 90 per cent. The figures in Table 1 seem t show that if the test for CRP is negative in chronic paranasal sinusitis, the chances for maxillary carcinoma are 1 50 However if a patient with inus t uble has a positive test for CRP the chances for maxillary carcinoma are 1 1

ZUSAMMENFASSUNG

Nachdem d C-reakti Protein 1930 im Blut von P eumonie-Pati nten ent deckt wurd hat man dieses I rot i bei t len Affektionen besonders bei In f ktionskrankheiten im kuten Stadium sowi bei rheumatischem Fi ber und bei frischem Herz f kt twa hundertprozentig festst llen kön en

I der Universitäts-Ohren N sen- und Halsklinik H lsinki wurd das eventu lle Vorkommen on C RP bei 819 mbula ten P tienten mit verschiedenen Affektionen unseres Spezialgebietes u tersu ht. C-RP wurde in 117 Fällen vorgef den, während 702 einen n gativen Befund hatten Die relati höchste Frequenz wurde be akuter Perit nsillitis, d. h in 93% festgestellt da ach f lgt das Maxillenkarzinom mit 90% Bei hronischer suppurativer Mittelohrentzündung, di immer und besonders beim Cholesteatom mit gewisser Knochenn krose verbunden ist, wa die Frequen des C-RP seh gering und betrug nur 2% Die Resultat zeigen ferner dass in Fällen on chronischer Paranasalsinuitis mit positivem C-RP im Serum ine 1 1 Möglichkeit von Karzinom der Nebenhöhlen vorliegt.

TABLE 1. *C reactive protein (CRP) in otolaryngological diseases. 810 cases*

Disease	No. of cases	Test for CRP	
		Positive	Negative
Chronic suppurative otitis media	112	2	110
Chronic suppurative otitis media with cholesteatoma	56	1	55
Acute mastoiditis	11	8	3
Otosclerosis	71	1	70
Microtia	11	—	11
Protruding ears	11	—	11
Menière's disease	[illegible]	—	16
Acute pansinusitis	20	4	16
Deviated nasal septum	51	1	50
Ozaena	11	—	11
Epistaxis	6	2	4
Nasal fracture	4	2	2
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CRP was positive in chronic tonsillitis in eight cases out of 30 and in all 18 cases of acute tonsillitis. Keitel, Diesner & Bannert (1964) prepared a review paper on CRP. Their own material consisted of 1058 cases, including 48 of otolaryngological origin. The purpose of this paper is to study the occurrence of CRP in ear, nose and throat diseases on the basis of a larger series than hitherto reported on.

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The results of CRP determinations in various ear nose and throat diseases are given in Table 1

SIZE OF THE HUMAN MASTOID AIR CELL SYSTEM

TAUNO PALVA and ANTTI PALVA
Oulu Finland

From the Department of Otolaryngology University of Oulu

The area of mastoid p eumatization was measured on 68 children's ears and after simple mastoidectomy th cavity volume was determined Another measurement was made utilising the dural tegmen and sigmoid plate laminae as limiting structures. This "laminal limits" figure cor responded well with cavity volume, but in small children the air cell area was significantly smaller Several f ctors are responsible for absent or poor pneumatization . If infection starts in infancy mastoid pneumatization does ot start or is rrested until normal conditions prev il in the middle ear Mast iditis in small children may result in marked new bo formation and subsequent sclerosis, and air cell f rmation fails to penetrate this barrier even if the middle ear is restored to normal. In a w ll pneumatized ear persisting infection in the mastoid process causes bliteratio of the cells already xisting and th end result resembles cases of primary arrested pneumatization

Pneumatization of the mastoid process has been th subject of lively debate in recent years while Dr Diamant and his pupils have put forward and defended their thesis that the size of the cell system is determined by genetic factors, the majority of other investigators claim that environmental factors play a decisive role in pneumatization.

It is generally agreed that the development of the mastoid air cells begins during the last few weeks of the fetal period This has been con firmed in dissections of newborn infant ears by Rüedi (1937) Bast & Forester (1939) and Ojala (1950) and radiologically by Welin (1941) and Rossmann (1938) In an extensive study of a total of 1000 ears of infants of varying ages, Rossmann (1936) found that in 25 per cent there was radiological evidence of air cells adjoining the antrum during the first four weeks after birth and at the end of the first month 43 per cent had some air cells. At the age of 6 months, all infants with healthy ears showed an antrum with adjoining air cells.

Several investigators have determined the size of the air cell system planimetrically from lateral x ray pictures as a function of age In a recent paper Kawamura *et al* (1963) reported that average air cell size in 1-year-old Japanese children w 3.06 sq cm In 2 year-old children the size increased to 4.33 sq cm, nd in 3-year-olds to 4.56 sq cm. At the age of 4, the average size was 5 10 sq cm, at 5 years 5.53 sq cm, and at 6

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TABLE 1 *Si e of air cell system (sq cm) as a function of age and sex (Rubensohn)*

	Age years														
	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15
Boys	4.2	4.5	6 1	7 1	9.3	8 2	8.7	10 7	11 1	12.3	9.3	8.2	10.6	11 1	10.6
Girls	4.8	5.2	6 9	7.2	8.2	10.0	9 1	11 3	11 6	13.2	11 7	11 6	11.5	11 6	11 4
Together	4 7	4 8	6.5	7.2	8 6	8 9	9 1	10 9	11 4	12.7	10 1	9 9	11 0	11 4	12.7

Not included in the original, but calculated from th individual figures

years 6 68 sq cm The most recent average planimetric figures were published by Rubensohn (1965) from the Halmstad clinic the children studied varied in age from 1 to 15 years, the total of ears being 413 These figures for boys and girls separately and together are reproduced in Table 1

It can be seen from the table that the growth in size continues to a certain extent in both sexes up to the age of 15 years The difference in size of the age groups between 11 and 15 is almost negligible however the maximum average for girls is highest in the 15-year-old group These figures do not justify Rubensohn s claim, a claim originally put forward by Diamant (1940) and later by Diamant Rubensohn & Walander (1958) that pneumatization in girls is terminated at the age of 10 and in boys at the age of 15

The actual volume of the air cell system has been measured in a few studies only Silbiger (1950) investigated 200 specimens of both left and right sided healthy temporal bones from cadavers each specimen was sliced in two the halves embedded in wax weighed filled with water and weighed again This weight difference naturally parallels the volume of water needed to fill the air cells, and average air cell volumes of 10.2 cc cm ± 2 0 in men and 17 6 cc cm ± 2 6 in women were obtained for a pair of ears The mean right and left side volumes were similar in both sexes Single healthy ears thus had an average volume of 9 cc cm

Another study was recently carried out (1965) by Flisberg & Zsigmond in an attempt to measure the air cell volume in normal ears utilizing gas volumetry An average volume of 12 22 ± 0 40 cc cm was obtained with a planimetric average of 12 09 ± 0 81 sq cm for the same ears These values correspond quite well with Diamant s average planimetric figure 12–13 sq cm The authors claim a high correlation between area and volume and one of their graphs suggests that these figures are numerically about the same in diseased ears too although both area and volume are then clearly smaller than normal

In Silbiger's series, the smallest air cell volume for single ears was 2.5 cc and the largest volume 20.8 cc In Rubensohn s study the maximum plani

metric area was 24 sq cm and the smallest was 0 sq cm. While Diamant's theory implies that absent mastoid pneumatization is a genetically determined, fairly frequent normal variant, other workers maintain that absent pneumatization is caused by exogeneous influences, notably by inflammation of the middle ear in childhood. An abnormally low pressure in the middle ear due to infection, or filling of the space with secretion, is commonly known to prevent the progress of mastoid pneumatization (Rüedi, 1937). Indeed, in cases with congenital anomalies, combined with absence of Eustachian tubes, air cells are found to be lacking although the parents may have normally pneumatized mastoids. Ojala's studies (1958) with chicken humerus also showed definite evidence of arrested pneumatization in the humerus if connections with its potential air cell space were surgically cut from the area with normal atmospheric pressure.

In a thorough study Rüedi (1937) divided pneumatization into two separate processes: preformation of the bony middle ear cavity and antrum occurring during early embryonal development is followed by pneumatization proper when air cells develop around the antrum and continue to grow towards the limits of the preformed bony cavities. The term dissociated pneumatization was used by Rüedi to denote a pathological process: it indicates that the air cells that had developed were still at a distance from the walls of the preformed bony cavities.

There is not very much disagreement regarding the size of the average normal air cell system, but pneumatization in infected ears is a highly controversial subject. Diamant having ascertained that the round, average air cell area was 12 + 3 sq cm in healthy persons, contrasted this with the average of 2.91 ± 0.27 sq cm in 275 chronically infected ears. This disparity he explained by saying that ears with a small air cell system are particularly prone to otitis media and that this is the very reason why selection occurs. He further supported his explanation by the fact that, in a series of 144 persons with acute otitis media, the air cell area was 0.71 ± 0.62 sq cm or only about three-fourths of the normal size.

What Diamant considered the cause of otitis media is considered by most other otologists, notably Tumarkin, as the result of otitis media. Thus otitic infections in childhood arrest normal pneumatization processes, and only when the middle ear infection has resolved and normal atmospheric conditions been restored, can air cell formation continue. So it is understandable that, in a series of cases with acute otitis media the average air cell size may be somewhat smaller than in a corresponding age group without any history of middle ear disease. Indeed, Tumarkin has shown that raising of the living standard of slum children with frequent infections results in a better relative state and causes a decrease in infections and increased size of the mastoid air cell system. It is also a common finding that in infants with mastoid infection, air cell formation fails to start; this was demonstrated for instance by Mérei (1949) who dealt with operated cases of nonresolved infection.

The finding of a remarkably small air cell system in chronic otitis is not at all astonishing considering the pathological processes at play. These have been studied extensively as early as during the first part of this century (Krainz, 1926; Mayer, 1928; Lange, 1928; Stewart, 1928; Singer, 1933 and others) before the antibiotic era by Friedmann (1955) and quite recently by T. Palva *et al.* (1964). There seem to be no essential differences between the findings on chronic ear histopathology.

In the initial stages, during the first week of mastoid infection, bony breakdown is the dominating process; the cellular septa are destroyed and granulation tissue and pus fill the infected area. Soon after this, generally in 14 days, the reparative processes start: new bone is formed in the granulation tissue from the nearby periosteum, and cellular septa grow in thickness. Bone destruction and repair then compete with each other and the end result in most cases is a sclerotic mastoid in which the air cells at the periphery have largely been converted into solid bone, or into bone containing small cells with thick septa, often filled with granulation tissue or collagen. The corticalis may attain a thickness of two centimeters and be of ivory hard bone; the air cells still present and measurable planimetrically are those adjoining the antrum and draining via the middle ear.

Naturally there are other causes differing from this general trend. In the presence of good resistance and/or relatively avirulent infection the healing processes may gain a rapid victory and after a temporary halt the pneumatization processes start anew. On the other hand, a virulent infection may swiftly traverse the bone and break through the bony laminae into various directions with serious complications.

Considering the histopathological course of the disease, it is therefore understandable that the air cell area in chronic ears shows much smaller values than is obtained in normal ears. In chronic ears of long standing the final measurable cell system may be much smaller than the one seen prior to infection and it is evident that without infection the cell system would have developed to normal size.

It has seemed to us that further information as regards the relation between the area and volume of the mastoid air cell system is obtainable from operated cases. Direct volume measurements can then be compared with the corresponding area measurements from roentgen plates. Furthermore, the deep area of possible pneumatization, bordered by the dural tegmen, the sino-dural angle, the sigmoid plate and the posterior ear canal wall, can be measured from the x-ray and compared with the volume data.

MATERIAL AND METHODS

We have included most of the cases hospitalized for mastoid infection and subjected to cortical mastoidectomy in the years 1958–1965. The material consists of 53 cases and a total of 68 operated ears. The majority

TABLE 2. *Size and volume of mastoid cell system in 68 children's ears*

Case No.	Age	Size sq cm Air cells	Size sq cm Laminal limits	Volume cc	Case No.	Age	Size sq cm Air cells	Size sq cm Laminal limits	Volume cc
1	4 mo.	No x-ray		1.7	35	2 y	1.6	2.1	2.8
2	4 mo.	No x-rays		1.5	36	2 y	0.6	4.8	6.5
3	4 mo.	0.6	1.2	1.1	37	2 y	2.4	3.9	2.8
4	4 mo.	1.0	1.7	1.8	38	2 y	1.7	2.5	2.8
5	5 mo.	0.3	1.4	2.0	39	2 y	2.8	2.8	2.8
6	5 mo.	0.4	2.4	1.5	40	3 y	1.9	3.0	2.0
7	6 mo.	1.4	3.1	1.4	41	3 y	0.0	3.0	4.0
8	7 mo.	0.6	0.6	1.0	42	3 y	0.0	1.5	2.4
9	7 mo.	0.2	0.9	1.0	43	2 y	0.7	1.9	1.6
10	7 mo.	0.5	1.3	2.0	44	2 y	0.7	1.3	1.4
11	8 mo.	0.9	2.3	1.7	45	2 y	1.1	2.2	2.2
12	8 mo.	2.6	2.8	2.4	46	2 y	1.2	2.3	1.6
13	9 mo.	No x-ray		2.0	47	2 y	0.0	1.9	1.6
14	9 mo.	No x-ray		1.4	48	3 y	3.3	3.9	2.6
15	10 mo.	2.2	2.6	1.9	49	3 y	2.2	3.5	2.3
16	10 mo.	0.8	1.9	2.0	50	3 y	3.1	3.1	2.7
17	10 mo.	0.5	0.8	1.5	51	4 y	0.1	3.6	2.8
18	10 mo.	No x-ray		2.5	52	4 y	6.0	3.2	4.0
19	10 mo.	No x-ray		2.3	53	6 y	1.2	2.4	[illegible]
20	1 y	1.8	3.4	1.5	54	5 y	7.6	5.0	2.5
21	1 y	1.0	3.0	2.0	55	6 y	2.0	2.0	1.8
22	1 y	0.8	2.0	3.4	56	7 y	6.5	4.5	5.2
23	1 y	1.5	2.8	2.2	57	8 y	1.6	3.0	2.5
24	1 y	2.5	2.6	1.6	58	8 y	0.7	4.5	3.2
25	1 y	2.4	2.4	2.8	59	8 y	2.1	2.1	2.8
26	1 y	2.2	2.3	2.3	60	8 y	1.8	2.0	1.8
27	1 y	0.7	3.1	1.8	61	8 y	6.7	8.0	8.0
28	1 y	0.0	3.0	2.0	62	10 y	0.0	3.4	3.0
29	1 y	1.3	2.2	2.6	63	11 y	1.9	2.6	4.8
30	1 y	1.8	2.6	1.8	64	11 y	13.8	5.8	5.0
31	1 y	2.3	2.3	2.2	65	12 y	14.7	5.4	6.0
32	1 y	2.0	2.0	1.2	66	12 y	1.7	2.7	4.2
33	2 y	0.0	2.8	2.8	67	13 y	7.8	6.1	5.0
34	2 y	2.9	2.9	2.0	68	14 y	2.4	3.1	3.0

f the patients were am ll children, under 3 years of age In 6 ears in the age group below 1 year no preoperative roentgen films were available, nd only lume measurement were made In addition, we included 20 chronic ears of adult patients treated by radical mastoid operation, and 20 consecutiv cases of clinical otosclerosis. All roentgen films were made in the n rmal lateral position

For p eoperativ planimetric measurements, the area of air cells, even if not air-containing, was outlined with a pencil, excluding the middl ear but including the ma t id antrum. Another measurement was subsequently

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worthy that very small air cell systems are found in older children examples are cases 62 (0 sq cm) and 66 (1 7 sq cm) The corresponding laminal limits, however are higher 3 4 and 2 7 sq cm, with volumes of 3 0 and 4.2 cc respectively

Study of the anamnestic data on the duration of otitis shows that the overwhelming majority of ears in this series had been the site of many repeated and often long standing infections, which, even in the older children, dated back to the first year of life Exceptions are cases 36, 54 [redacted] 65 and 67 in which the ears had been healthy except for the present virulent attack resulting in acute mastoiditis and subperiosteal abscess in a matter of two or three days In these ears the air cell system measured by any of the three standards, was found to be much bigger than in the main group Older children with long standing infection (e.g cases 62, 63, 66) however showed air cells only around the antrum, the mastoid being otherwise sclerotic The volume in these cases was also occasionally small there was no need to do extensive drilling since the sclerotic new bone had bliterated all pe laínal cells.

In 20 chronic ears subjected to radical mastoid operation, the preoperative average air-containing cell area measured 4.8 ± 5.3 sq cm. When also obliterated cells were included in the measurement, the average area increased to 6.7 ± 5 1 sq cm The corresponding laminal limits figure was 8 6 ± 2 1 sq cm Postoperatively the area of the operative cavity averaged in 9.3 ± 4 7 sq cm, while the average volume was 5.5 ± 2 0 cc.

In 20 ears with otosclerosis, the pneumatized area measured 20.2 ± 5.5 sq cm, and the laminal limits area was clearly smaller 10.5 ± 3.5 sq cm. However among these 20 consecutive cases there were 2 patients who had had several attacks of otiti media in childhood The middle ears eventually became normal but the mastoid healed with sclerosis. In these ears the pneumalized rea was clearl maller (1 and 3 4 sq cm) than in cases with no history of middle ear infections the corresponding laminal limits figures were close to the verage viz. and 10.5 sq cm

DISCUSSION

Comparison of the three groups of figures in Table 2 reveals certain interesting finding Although, in the young age groups, the average figures indicating the size of the air cell and that of the bony space, limited by Laminae are f the sam magnitude th latter figure is significantly larger than the f rmer in infants and in 1 year-old children In 2 year-old children there is no statistically ignificant difference between the two averages (Table 3) Th laminal limit figure e pres ing the area in sq cm, in all groups parallel that f volume in cc (Fig 1 Table 3)

These d ta seem t indicate clearly that if otitis st rts early pneumatization processes are rrested at th outset, and the preformed bony space, indicated by the figures of lamin l limit or of v lume is clearly larger

TABLE 3 *Average size and volume in three age groups*

Age	No. of cases	Average size (sq. cm) Air cells	Laminal limits	s.e. of means	Significance level (*P*)	Volume cc
<1 year	13	0.9±0.8	1.7±0.8	0.3	0.0125	1.7
1–2 years	13	1.6±0.8	2.6±0.4	0.35	0.0003	2.0
2–3 years	15	1.8±2.3	2.6±1.9	0.[illegible]8	0.15	2.6

made utilizing the bony laminae and the ear canal wall and the mastoid tip as extreme limits and the size of this area was again determined with the planimeter. In chronic adult ears two measurements were made preoperatively: the area of air-containing cells and the area in which air cells (even if occluded) were thought still to be present were measured. Roentgen examination was repeated postoperatively and the area of the operative cavity was outlined and measured with the planimeter. After completion of the simple mastoid operation and creation of a cavity, the patient's head was turned sideways and the volume of the mastoid cavity determined with saline solution. This measurement of course also included the mastoid antrum but excluded the middle ear and ear canal. In radical mastoid cavities, on the other hand, volume measurement included the middle ear and the bony part of the auditory canal. The experimental error on repeated measurements on children's ears did not exceed one-tenth of a milliliter.

RESULTS

The cases with simple mastoidectomy are arranged according to age in Table 2 and the three figures obtained on the basis of different measurements are shown side by side. The average values for the largest three age groups are also shown in Table 3.

In the group of 13 infant ears, the measurable air cell area is small with an average of 0.9 sq. cm. The laminal limits area is nearly twice as large, 1.7 sq. cm; the volume measurements correlate very closely (average 1.7 cc) with this figure.

A similar relationship is seen in 13 ears of 1-year-old children in whom the average air cell area increased to 1.6 sq. cm. The average laminal limits areal figure is 2.6 sq. cm; the volume measured is somewhat smaller, 2.0 cc. In 2-year-old children the figures are of the same general magnitude but the laminal limits area and the volume show the same average 2.6. The groups of older children are so much smaller that average figures cannot be usefully employed. There are individual cases (3-year-old group) in which all three figures are of the same order and some in which air cell size greatly exceeds both the laminal limits value and the volume. This is particularly evident in the two 4-year-old children as well as in one child of 11 years and another of 12 years. It is also note-

Fig. 2. A case of right-sided acute mastoiditis in a 9-year-old girl. In the healthy left ear (a) there is extensive pneumatization (cell area 33.1 sq cm, laminal limit 14.4 sq cm). In the right ear (b) the outlines of the cell system are still seen in spite of extensive bony breakdown (cell area 32.8 sq cm, laminal limit 11.8 sq cm, volume 14 cc). There was marked bone destruction but also some osteoblastic activity and new bone formation even if the history was no longer than 7 days.

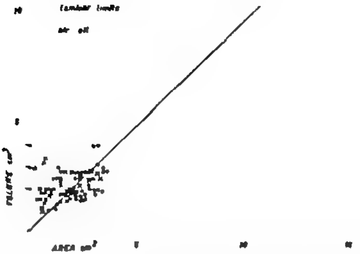

FIG 1 Relation of area (sq cm) to volume (cc) in 68 simple mastoidectomies in 53 children It appears that very small air cell areas correlate with clearly bigger volumes, while the volume is of the same order as the laminal limit figure In some well pneumatized ears with acute mastoiditis, however the air cell area is much bigger than is the corresponding volume or the laminal limits are

than the pneumatized area In growing children after initial periods of normal pneumatization the two areal figures may not show statistically significant differences (2 year-old group) although the area of pneumatization is smaller than the other values, and much smaller than the values in normal series

The parallelism between the area of laminal limits in sq cm and the volume in cc is evident also in older children, but our case material is limited in these groups In a few cases however the area of the air cells clearly exceeds the other two figures even doubly Thus in two of the older children the air cell area was over 13 sq cm whereas the direct volume measure was 5 and 6 cc This is explained by the fact that although pneumatization may be extensive in a lateral x ray it lacks depth in the area over the sigmoid plate, being often only a few millimeters in thickness accordingly its contribution to the volume is limited Only in those cases in which the sigmoid plate is situated deep down can the measured volume reach figures exceeding 10 cc

The volumes obtained earlier in normal adult series by Silbiger (about 9 cc) and Flisberg *et al* (about 12 cc) are clearly larger than those reported in this study One of the reasons is naturally that we dealt with children's ears the few operations performed on fully pneumatized non infected adult ears e.g because of traumatic facial palsy show larger volumes reaching the figures of Silbiger The maximum obtained by us is 22 cc Since the study of Flisberg *et al* with the gas volumetric method included also the tympanum and the bony Eustachian tube there is no marked difference in the magnitude of the figures

Another explanation of the smaller volume figures in adult cases subjected to radical mastoidectomy is that the area above and posterior to

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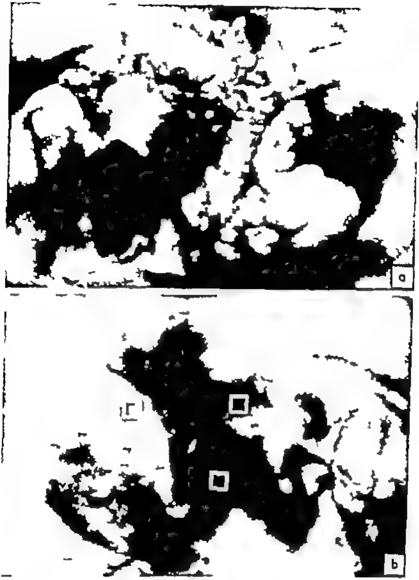


Fig 3 A case f hronic titi (set t 7 y rs) in t ight ear f a 50- r-old f rmer whose left ear had alwa be n n rm l Pn um ti ti n i w ll devel ped in the left ear (*upper*) and very poor i t ight (open at cell 1 1 sq c blit rated cell 7 4 sq cm, laminal limit 8.0 q cm) At perati oblit ted cell were f und at the mast id tip and po teri r to t igm id i n whi l pro ed th t bsence f pneumati ti n was due to a sclero ing proc i a m t id, w ll p um ti ed pri r t infecti n The v lum f the perati n ca ity w 5.6 cc d th re f the ca ity 8.0 sq m Squares indicate th ites f tissu pecim f hi t logi l tudy

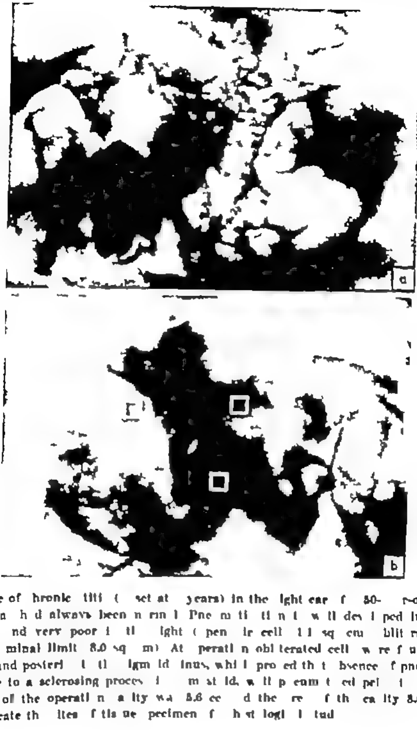
the sigmoid sinus has failed to be pneumatized because of infection or the air cells in this area and at the mastoid tip have been transformed into solid bone which has not been drilled away at operation The bony cavity created operatively thus corresponds quite closely to the laminal limits used to indicate the deep area capable of becoming totally pneumatized

Flisberg *et al* are inclined to think in accordance with the original idea of Diamant that an ear with a small air cell system is much more

Fig. 4. Coal ... of totally obliterated ... cell from the post-sigmoid area (Fig. 3). There is ... typical cholesteatoma granuloma, still showing the rounded contours of an air cell. 25

likely to contract otitis media if the tube becomes "locked", since the reservoir of air in the air cell is smaller than in a well pneumatized mastoid. We quite agree, and so do most students of pneumatization, that a poorly functioning Eustachian tube is the key to the problem, but we fail to recognize how this can possibly be linked up with the size of the cell system to such a degree. On the contrary, one would say that, when repeated and often long-standing nasopharyngeal infections cause obstruction of the tube and generally infect also the middle ear, the ear stands a very poor chance of being pneumatized as compared with a healthy ear. The middle ears in our 2 cases of otosclerosis with arrested pneumatization due to ... serous otitis media as children, functioned equally well as the contralateral ear with normal pneumatization.

In the case of sclerotic, poorly pneumatized mastoids there appear to be two main factors that contribute to this end result. One is the presence of a generally long-standing infection in the nasal pharynx in childhood, leading to negative pressure in the middle ear, serous otitis media, and infection, all causing a halt in air cell formation. Another is otitis media and mastoiditis starting at any age without a significant previous history



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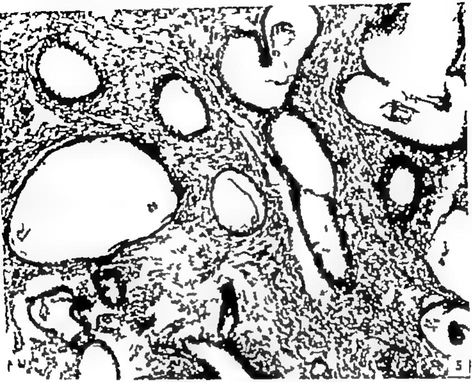

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FIG. 6. Bone chip from the area of the mastoid tip shown in Fig. 3. Microscopically changes typical of a sclerosing mastoid are seen, with irregular lines of apposition. The remaining air cells are very small and only microscopic ×75.

of disease A fairly well pneumatized mastoid will then become the site of simultaneous bone destruction and new bone formation processes the air cells already existing may be filled with granulation tissue and later collagen, and may eventually be converted into dense acellular bone In the later stages air-containing cells are not seen except possibly in the vicinity of the antrum where they remain open longest If mastoiditis occurs at an early age and the ear heals without operation the lying down of new bone causes the development of a sclerosed mastoid (T Palva *et al* 1964) which effectively prevents further pneumatization even if the normalized tube and middle ear would otherwise allow this process to continue

If one measures the air cell area at the sclerotic stage before operation, without knowing the size of the air space before the onset of disease the figure may be misleading and only represent the sclerotic mastoid, which we know has a small air cell area Fig 3 illustrated such a case the healthy left ear showed normal pneumatization while the diseased ear had arrested pneumatization microscopic examination however revealed occluded air cells new bone formation, and cells filled with collagen The finding of absent pneumatization thus indicates only the end result in a previously pneumatized ear a result of mastoid infection and entirely unrelated to a genetically determined lack of pneumatization

In another paper Flisberg *et al* suggest that an air chamber should be created in the mastoid by operation in cases lacking accessory air spaces. This is contrary to all clinical experience in chronic ear surgery In simple mastoidectomies we have (T Palva *et al* 1964) for 15 years occluded the antrum and separated it from the middle ear by means of a musculoperiosteal flap In spite of this, there have been no difficulties in achieving postoperative good hearing if the adhesive changes in the middle ear are not extensive enough to prevent the restoration of hearing Even without a musculoperiosteal flap the antrum and its extensions will be filled with collagen in the great majority of cases and will not provide any accessory middle ear air space

Similarly our present series of over 600 cases testifies that in chronic ear surgery routine occlusion of the antrum and its separation from the middle ear does in no way reduce the good functional end result provided the middle ear spaces are normal If the middle ear is grossly diseased and tubal function poor the presence of an accessory air space in the mastoid cannot help in the re-establishment of normal middle ear function adhesions are likely to form if no permanent separation, e g a paraffin prosthesis, is employed

FIG. 5 Biopsy from the perla tral rea whi h, in Fig 3, h wed some radi tra lucency Microscopically absence f bo i noted a d it place h bee t ken b dense fibro connecti e tissue containing many pithell m ll ed m ll ca ities, represe ting re t of former air cell epithelium. × 150

Fig. 6. Bone chip from the area of the mastoid tip shown in Fig. 3. Microscopically changes typical of sclerosing mastoid are seen, with irregular lines of apposition. The remaining air cells are very small and oval. Microscopic × 175.

Regarding mastoid pneumatization the evidence obtained in this study of planimetric and volumetric measurements seems to warrant certain conclusions If infection starts in infancy there is arrested pneumatization at the time of operation and the air cell area is clearly smaller than is the area limited by laminae, that should be pneumatized at that age Correspondingly the volume is also bigger than the areal figure If these ears heal without operation new bone formation with subsequent sclerosis may form an effective barrier to further pneumatization even if conditions in the middle ear become normal

If infection starts later after normal periods of pneumatization and the patient is operated on because of mastoiditis, the area occupied by air cells, even if not air-containing by reason of infection is clearly larger than are the figures for laminal limits or volume If the disease becomes chronic and continues for many years then much of the peripheral originally pneumatized area is transformed into solid bone with no air cells the planimetric air cell figure then no longer represents the area at one time pneumatized but only expresses the end result To use this figure as a measure of pneumatization is totally misleading Therefore we feel that the ideas earlier expressed by Rüedi, Tumarkin and many others, to the effect that exogenic factors are dominant in mastoid pneumatization are justified It would not be feasible to assign a decisive role to endogenic in utero factors It is obvious, however that some endogenic factors are involved the position of the temporal dura and that of the sigmoid sinus, which are more or less endogeneously determined, affect particularly the volume measurements but only in a very rare case can their influence be great enough to cause absence of mastoid pneumatization

ZUSAMMENFASSUNG

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Regarding mastoid pneumatization the evidence obtained in this study of planimetric and volumetric measurements seems to warrant certain conclusions If infection starts in infancy there is arrested pneumatization at the time of operation and the air cell area is clearly smaller than is the area, limited by laminae, that should be pneumatized at that age Correspondingly the volume is also bigger than the areal figure If these ears heal without operation new bone formation with subsequent sclerosis may form an effective barrier to *further pneumatization* even if conditions in the middle ear become normal

If infection starts later after normal periods of pneumatization and *the patient is operated on because of mastoiditis*, the area occupied by air cells, even if not air-containing by reason of infection, is clearly larger than are the figures for laminal limits or volume If the disease becomes chronic and continues for many years, then much of the peripheral originally pneumatized area is transformed into solid bone with no air cells the planimetric air cell figure then no longer represents the area at one time pneumatized but only expresses the end result To use this figure as a measure of pneumatization is totally misleading Therefore we feel that the ideas earlier expressed by Rüedi Tumarkin and many others, to the effect that exogenic factors are dominant in mastoid pneumatization are justified it would not be feasible to assign a decisive role to endogenic in utero factors It is obvious, however that some endogenic factors are involved the position of the temporal dura and that of the sigmoid sinus, which are more or less endogeneously determined affect particularly the volume measurements but only in a very rare case can their influence be great enough to cause absence of mastoid pneumatization

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POSTURAL PERCEPTIONS AND COMPENSATORY DISPLACEMENTS OF THE EYE IN RESPECT TO A PRESENTED FORCE FIELD

Synchronous Three Orthogonal Registration

U. Brandt and E. Fluur
Stockholm, Sweden

From the Laboratory of Aviation Medicine (Head: Prof. H. Bjurstedt), Karolinska Institutet, and the Department of Otolaryngology (Head: Prof. C. A. Hamberger), Karolinska Sjukhuset, Stockholm 60

The method described allows qualitative and quantitative registration along three axes (X, Y and Z) of the apparent change in space of an observed object watched by an individual deprived of visual references while he is subjected to force fields of varying direction and of varying magnitude. By means of a synchronous infrared filming technique it is also possible at each moment of the procedure to determine with good approximation the directional changes of the eye in the same three axes, and thus to correlate them with the recorded perceptions. The validity of the various parts of the produce is subjected to critical appraisal.

When a subject is exposed to a resultant force in a test centrifuge in total darkness, he notices under suitable conditions systematic apparent changes in position of a barely supraliminal visual stimulus. It is feasible by means of infrared (IR) filming to determine both qualitatively and quantitatively, and at any moment, the relative change in position of the eye. These findings can then be correlated to the subjective data recorded. Synchronous registration along the three axes of these two types of information—indication of the change in position and directional ocular change—when the subject's head is submitted to a well-defined force field is the aim of this new procedure, which is an elaboration of techniques described by several authors (Witkin 1950, Clark & Graybiel 1951, Graybiel 1952, Graybiel 1956, Brandt 1957, Brandt 1962, Miller & Graybiel 1963, Brandt 1964).

1. Technique of Stimulation

Procedure for positioning the subject (Fig. 1)

The centrifuge is completely covered by a darkroom arrangement. An ordinary pilot's seat is mounted in the centre of the horizontal platform

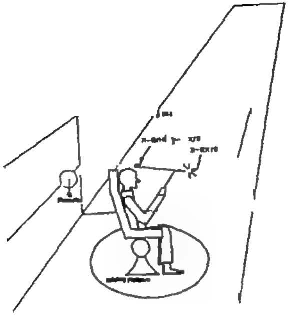

FIG. 1 The horizontal platform with the test bject in the da kroom. I front of him, the indicator cross. The seat, mounted universal joint, nd the mov ble pl tform permit all variations in the subject position referred t the phy ical ertical and t the centre of the centrif ge

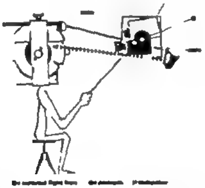

FIG. 2. Test subject with supporti g and rigid fi tion devices (chi ad head pport, plates which ca be screwed ide y in both directions, girdl t constrai the tru k, etc) Indicator (*I*) camera (*C*) and Ill mination box (*B*)

at the outer end of one of the centrifuge arms A universal joint allows the seat to be turned and tilted in every plan above the platform As this I also movable around the axi of the seat, it permits every possible varia tion for positioning the subject in space and in relation to th resultant force presented (Figs. 1 and 2) Various positions in space and in respect t the field presented are possible

A When the subject is facing centripet lly (HCp) and he is sitting in

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When a subject is exposed to a resultant force in a test centrifuge in total darkness, *he notices under suitable conditions systematic apparent* changes in position of a barely supraliminal visual stimulus It is feasible by means of infrared (IR) filming to determine, both qualitatively and quantitatively and at any moment the relative change in position of the eye These findings can then be correlated to the subjective data recorded Synchronous registration along the three axes of these two types of information—indication of the change in position and directional ocular change—when the subject s head is submitted to a well-defined force field is the aim of this new procedure which is an elaboration of techniques described by several authors (Witkin 1950 *Clark & Graybiel 1951 Graybiel*, 1952 Graybiel, 1956 Brandt, 1957 Brandt 1962 Miller & Graybiel 1963 Brandt, 1964)

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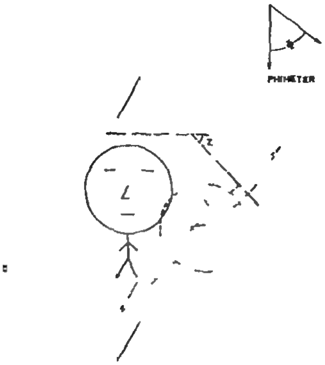


FIG. 4 Test subject heading forwards (*HF*) in erect positi n, the median sagittal plane being introduced as plane of reference. I thi position, the interest is concentrated on the pparent changes in the rolling plane (*Z* axis)

Since this pendulum is always placed *at exactly* the same distance from the centre of the centrifuge as is the subject s head, its deflections will provide at least three items of information, i.e the current direction of the force field and especially its *relative* angl if incidence to any of the above-mentioned head planes of reference the magnitude of this field (resultant G) and also, approximately the amount of angular acceleration delivered during a given time The precision and reliability of this instrument should *therefore* be subjected to accurate tests. The reason for this check is that most of the test centrifuges ha e their activity indicated in revolutions per *unit of time* but in this particular test procedure it is more uitable to express directly and record this activity in the angl ϕ against a time parameter

Table 1 shows the mean and S.D of 15 angle readings t the same rotation steps. It can be seen that the S.D is fairly mall, and in each stage less than 1 It can also be seen that the deflexions of the phimeter as a function f the angular velocity of the centrifuge vary within acceptable limits, and can thus be accepted as a parameter

This registration is made photokymographically by means of a poten-

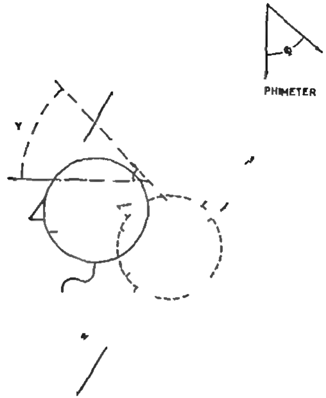


Fig 3 Test subject heading centripetally (*HCp*) and in n erect positi n. In thi posi tion, the change (subjectiv) occur chi fly in a headward direction (Y axis) and the fro tal plane i selected s pl ne of ref renc

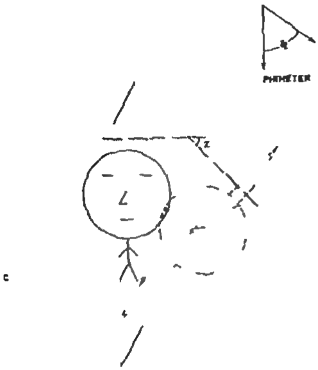
an erect position (chair not tilted Fig 3) slow acceleration of the centri fuge induces a sensation of being "tilted outwards" at the same time as the visual stimulus presented seems to move upwards (along the Y axis) Both with respect to the acting resulting force and to the subject s estimates, the (vertically set) frontal plane is suitable as reference plane

B When the subject faces forwards (HF) in the direction of motion of the centrifuge seated vertically he will chiefly experience a sense of sidewise and outward tilt (*Z* axis) with the same effect on the visual sti mulus (Fig 4) The (vertically set) median sagittal plane can be used as plane of reference

Furthermore the testing procedure permits great variations in the initial position of the subject and particularly of his head He can be tilted back wards, forwards sideways and positioned with his back against the centre of the centrifuge (heading centrifugal = HCf) in varying degrees When tilted the amount of tilt is given as the angle formed by the plane of reference to the physical vertical

Recording of accelerative conditions

The actual direction (angle Φ) of the stimulus, i e., the resultant force is expressed by means of the phimeter which has been described in previous articles



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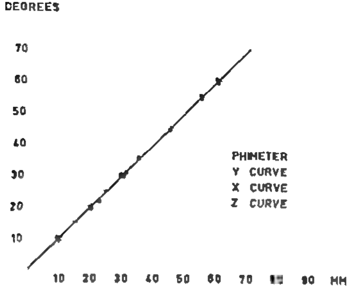


Fig. 5 Calibration test f the f ar photokymographic curves ("phimeter Y 1 and Z) The tests sh w xact linearity between the distanc s measured on the recording t pe (the ordinate) and the angles directly determined by the goniom ter (the abscissa)

tiometer and mirror galvanometer This implies that the photometric writer must be calibrated When the centrifuge is at standstill the writer is set at 0 By direct goniometer reading in conjunction with the change in direction of the pendulum it is possible to check that a certain angle of the phimeter is always followed by an identical movement of the photokymographic writer Fig 5 ("phimeter) shows an exact linear relation between angular measurements and measured distances, which indicates good reliability in this respect

Table 1 *Variation of angle Φ at a giv n rpm (radial distance of phimeter 7 25 m)*

= 15

rpm	Φ Mean	s.D
0	0	0
2	1 90	0 15
4	8 01	0 25
6	16 33	0 31
8	30 26	0 85
10	41 [illegible]	0.80
12	53 91	0 70
14	63.0	0 16
15	68.5	0 81

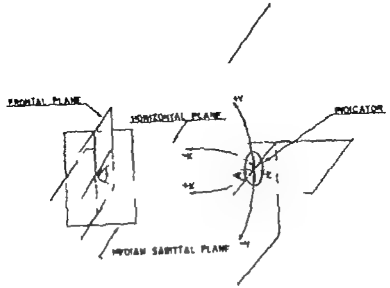


Fig. 6. Sketch showing free movements along the three axes of the indicator and the planes where these movements occur. The corresponding denotation is applied for the movements of the eye.

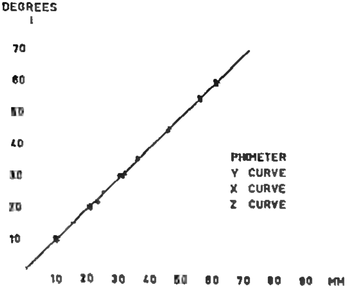
2. *Recording Techniques*

Registration of the subjective response

The combined experimental aims required improvements in the technique previously described. In this, the tests were based solely on the apparent deviation (in the rolling plane) of the indicator from the horizontal. When returning the indicator to a "horizontal" position, the subject indicated a certain angle which expressed his opinion of the change in respect to a certain direction of the resultant force.

These intermittent settings were replaced by a continuous recording, synchronous with data from the phimeter. The following psychophysical precautions were taken. To avoid the subject being influenced by the position of the indicator in stating his estimations, an automatic switch turned the light source of the indicator on and off (3 sec light and 3 sec darkness). During the period of darkness, this was offset by the examiner (these offsets were naturally not recorded). Consequently the subject was not influenced in his actual estimate by his previous adjustment.

It is known that the subject—in addition to the change in the view of the horizontal—experiences other sensations of a change in space of the observed object (sideways, head- and footwards). This made it desirable to record these displacements also along the two other possible axes. The recording apparatus was therefore equipped with two more pivoting shafts, both placed at the point of support of the indicator arm, slightly in front of the eyes' central axis (Fig. 2). This gave the indicator unit a greater



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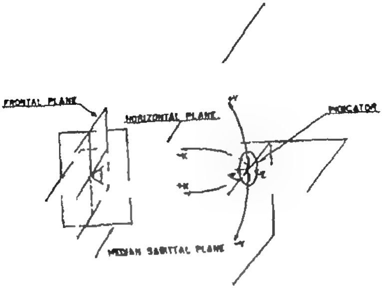
8	30 26	0 85
10	41 10	0 80
12	53 91	0.76
14	63.0	0 10
15	60.5	0 81



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It i known that the subject—in addition to the change in the view of the horizont l -experiences ther sensations of a change in space of the observed object (sideways, head and footwards) This made it desirable t record these di placements also along the two other possible axes. The recording apparatus was theref r equipped with two more pivoting shafts, both placed at the point of upport of the indicator arm, slightly in front of the eyes central xi (Fig. 2) This gave the indicator unit a greater

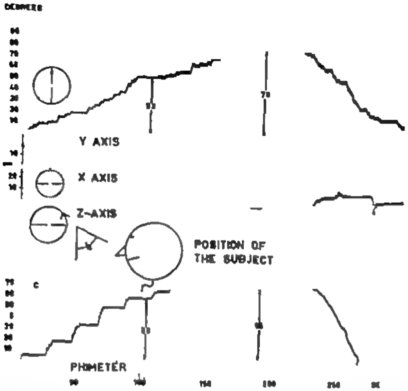

FIG. 7 Recorded subject's response of the test object heading centripetally (HCp) and without initial tilt. At the bottom is shown the angular deflexion of the phimeter. The arrows indicate the direction of the apparent displacement and the X, Y and Z curves represent this displacement in the respective axis.

freedom of movement within the field of vision (Fig. 6). Thus, the procedure indicates the apparent displacements and directional changes of the visual object not only in the rolling plane (Z axis) but also head- and footwards (Y axis) and sideways (X axis).

The apparatus for transferring the subject's indications (i.e., his action in restoring the indicator to the initial horizontal position) operates along the same lines as the phimeter. Direct measurements must be carried out by using goniometer and level to check the consistency of the indicator position (expressed in angles referred to an initial position) and the corresponding photokymographic registration. Here, too, accurate calibration is necessary to ensure that a given angular displacement of the indicator along any of three axes is exactly equalled by a proportional displacement of the recorder. Fig. 5 shows that this occurs in the three possibilities X, Y and Z.

Interpretation of the subjective recordings

Independently of the selected position in relation to the centre of the centrifuge, the subject experiences an apparent movement or directional change of the observed indicator. He is instructed to keep this in the position in space it occupied before the centrifuge was started, i.e., to restore

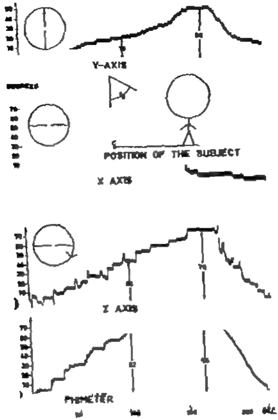

FIG. 8. Recorded subjectiv response for test subject heading forwards (*HF*) nd in ertical position. At the bottom, the stepwise increasing angl Φ ("phimeter") The arrow indicat that the pparent turn i the rolli g plane (*Z* axis) progresses in lockwise direction nd that the subject eports movement headwards (*Y* axis) There are practically no changes sidew y (*X* axis) All these reports are recorded quantita th ly

the indicator i its initial position His readjustments originate in fact from two *concepts* his opinion of "horizontal and his "initial" position, and his responses are represented on the subjecti e recordings by the three curves, denoted s *X* *Y* and *Z* The direction of each movement or direc tional change is indicated by using suitable *signs* in accordance with the system 2 in the NASA Life Sci nce Data Book, June 1962. Consequently a movement in a h adward o in an outward direction or a turn in a clock wise direction, is registered as a "positive ch nge. A footward or an inward directed apparent movement, r a turn in a counterclockwise direc tion is denoted by a negative sign (Fig. 6) Information about these sub-jective changes i given in Fig. 7 (subject heading centripetal chair rect) and Fig. 8 (subject heading forwards, chai erect) where the three curves (*X* *Y* and *Z*) represent, both in direction and quantitatively the various

movements and directional changes of the indicator in relation to an initial horizontal position which he has set before the start

When observing such a curve, one should note that the recording procedure also gives information about the possible oculogyral illusion (V curve) Thus it reveals whether there has been any angular acceleration sufficiently strong to stimulate the semicircular canals, and produce a sensation of turn

An approximate determination can also be made of the amount of angular acceleration delivered between two times during a test period on the basis of measurements on the phimeter curve (Φ)

Finally the subjective recordings permit the mutual relation to be followed between the responses and the stimulus (the resultant force defined by its direction and its magnitude) referred to the same plane of reference of the head

Objective registration of the ocular changes

A film camera directed on the *left eye* records its behaviour during the various phases of the test procedure, to introduce an objective additional recording element Because total darkness is an absolute requirement the filming is made with IR sensitive film The position of the camera is shown in Fig 2 We used a Paillard H 16 RKV with a parallax free finder of mirror reflex type The optical unit consisted of a 2 8/75 mm objective with a 20 mm adapter The opening was set at 8 and the speed was 24 squares/sec corresponding to an exposure of 1/45 sec. The distance between the focal plane and the left eye was 30 cm

The camera was provided with an electric motor which could be remotely switched on and off from the control room a fact of the greatest importance for identifying the ocular changes with the subjective recording

The following arrangements were made to meet the basic prerequisites of filming in total darkness An illumination unit (Kobolt SR 1 with a quartz iodide bulb and constant colour temperature) emitting a light of 26 000 lumen was installed in a light proof box with a hole to let through light The hole was covered with an infra filter (Kodak Wratten Infra filter no 87) which absorbed all visible light The infrared sections of the light spectrum which were reflected by the eye and its surroundings, activated the film (Kodak Infra High Speed 16 mm) To eliminate any disturbing eye reflexes, the "illumination struck the eye at an angle of 45

Control of eye fixation and standardization of the initial position (absolute zero)

Recent authors (Sullivan *et al* 1958 Graybiel & Woellner 1959 Miller 1962) have pointed out that the earliest general criticisms of studies involving eye displacement dealt with the apparent lack of adequate control of eye position, or complete disregard of it

TABLE 2 *Variation of Resultant G in function of angle Φ at constant velocity*

Angle (degrees)	Resultant G	Angle (degrees)	Resultant G
0	1.0	30	1.15
2.5	1.0009	35	1.2
5.0	1.003	40	1.3
7.5	1.008	45	1.4
10	1.01	50	1.5
15	1.03	55	1.7
20	1.06	60	1.9
25	1.10	65	2.3
		70	2.8

To eliminate this possible source of error the subject is told before each test and while in the erect position (chair not tilted) to look straight forward Moreover when black-out and adaptation to this condition have taken place he is instructed to keep his gaze with the foveal fixation directed on a small dot (luminiscent material) on the upper edge of the camera objective While fixing his *left eye* in this direction, he sets the movable indicator horizontally and at a corresponding level in front of his *right eye* These points of departure of both the eye and the indicator may when graphically presented, be defined as "absolute zero All subsequent measurements on the recorded curves and on the film are referred to the starting points and to the frames obtained under these conditions.

Although during the tests the subject is deprived of all visual stimulus, both the dot on the upper edge of the objective (left eye) and the indicator (right eye) deliver very small quantities of light, sufficiently low to avoid visual orientation to the surroundings, the subject is instructed to keep the left eye foveally fixed on the dot, when the filming is performed Concerning the technique of readjustments, the procedure is submitted to small variations, which will be more exactly described in each experiment

Measuring technique

In order to obtain exact measurements of the ocular changes along the three axes, a line joining the inner and the outer canthus of the eye is selected as reference The measurements are performed directly on the film in a viewer magnifying 400 times. To obtain these results, it is necessary to refer all changes to a "photograph of reference on transparent material, which represents for each subject and for each experimental series the absolute zero for this subject in a given position

When determining the changes which have occurred between two frames, the technique is different for the three axes. The simplest way to measure the displacement along the X and Y axes is to superimpose the photograph

movements and directional changes of the indicator in relation to an initial *horizontal* position which he has set before the start

When observing such a curve one should note that the recording procedure *also gives information about the possible oculogyral illusion* (V curve) Thus it reveals whether there has been any angular acceleration sufficiently *strong to stimulate the semicircular canals*, and produce a sensation of turn

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ment along one of the two axes Y or X reduced to the anatomical eye is obtained from the formula

$$\alpha = \frac{360}{2\pi \cdot r} A = 6 \cdot A$$

where r is the average radius of the human eye and A the real displacement reduced to the anatomical eye.

It is scarcely possible to define the radius of the eye exactly in a living person, and this is the first reason why an approximation has to be made. The other intermediate steps in the computation are fully secured, how ever as is the direction of the torsion obtained

Synchronization of the subjective recordings and the ocular changes

To conclude, the parallelism between the phimeter and the subjective recordings does not raise any problems. The synchronization of the registered ocular changes and the other data on the other hand, has to be checked. This is done by switching on and off the lamp of IR "illumina tion by a remote-control switch. This procedure is clearly marked on the film at the same time as it is marked or indicated on the recorded curve. Since these markings re easily demonstrable on the film and on the curve the regi tered ocular change in relation to the recorded curve can be localized with great accuracy

RESUMÉ

Les auteurs décri ent une méthode permettant l'enregistrement suivant trois xes (X, Y et Z) d déplacement dans l'espace d'un obj t faiblement visible présenté à un sujet pri é d a tre part de toutes références visuelles, tandi que celui-ci est soumis à des champs de force de direction ■ de puissanc va iables. Par le moyen d un technique de filmage à l'infra-rouge il est possible à chaque moment de l'expérience de déterminer d une manière pproximative les change ments de direction (mou ements de compensation) de l'œil sui ant les mêmes trois axes, et par là même d mettre en rapport ces changements ec les per ceptions de déplacement enregistrées simultanément dan les mêmes conditions dynamiques. La méthod est soumise da s ses différentes parties à une évaluation critique

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of reference on the enlarged picture, and then to compare the distance of the pupillary centre to the invariable line of reference on the two pictures. This technique is based on the fact that the pupil is maximally dilated in the total darkness where the tests are being made. According to a system of coordinates the displacements of the pupillary centre which occur head or footwards can be referred to the line of reference and the changes occurring sideways to a line at right angles to the former As the quality of the pictures is generally excellent the changes can also be determined by superimposing and comparing recurring details in the sclerae iris and pupil boundary

When determining the torsional changes in the rolling plane, the measuring technique is also based on the fact that the pupil is maximally dilated and in addition not absolutely circular in shape In fact two diameters of one and the same pupil placed at right angles to each other reveal a difference of about 1 mm This difference, which is clearly visible when the picture is enlarged added to the recurring details in the sclerae iris and pupil permits an adequate comparison of the rolling changes which have occurred between two frames A certain roll from one enlarged picture A to another B is directly determined by superimposing the two pictures exactly and then measuring the angle formed between the line joining the two invariable landmarks.

Conversion of the measured displacement of the pupillary centre into torsional movement

In order to compare the ocular changes with the recorded subjective data it is desirable to be able to work with the same system of units The phimeter deflexion the subjective responses and the ocular torsions in the rolling plane are obtained without any special computations directly in angular units (degrees) This does not apply to the head and footward and sideways displacements of the eye which are obtained as distances on the greatly enlarged pictures By means of the knowledge of the magnification from the anatomical eye to picture the measured values can be reduced to the dimension of the eye and will present the real ocular displacement with great accuracy but in a plane whereas these changes actually represent torsional movements

With slight variations, the human eye constitutes an almost perfect sphere having an average radius of 11–12 mm The measured displacement of the centre of the pupil from one picture to another reduced to the anatomical eye (distance A) can be equalled to the arc length in the spherical surface An angle α corresponds to this arc length and constitutes the ocular torsion along the respective axis As this angle is assumed to be very small there is in fact an inappreciable difference between 1 and the corresponding arc length

The torsion of the eye corresponding to a certain measured displace-

ment, along one of the two axes Y or X reduced to the anatomical eye, is obtained from the formula

$$\alpha = \frac{360}{2\pi\ r}\ A = 5\ A$$

where r is the average radius of the human eye and A the real displacement reduced to the anatomical eye.

It is scarcely possible to define the radius of the eye exactly in a living person, and this is the first reason why an approximation has to be made. The other intermediate steps in the computation are fully secured, however as is the direction of the torsion obtained

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RESUMÉ

Les auteurs décrivent une méthode permettant l'enregistrement *suivant* trois axes (X Y et Z) du déplacement dans l espace d u objet *faiblement visible* présenté à un sujet privé d autre part d toutes références visuelles, *tandis que celui-ci est soumi* à des champs de force de direction et de puissance variables. Par le moyen d'un technique d filmage à l'infra-rouge il est possible à chaque moment de l expérience de déterminer d une manière approximati e les changements de direction *(mouveme ts de compensation)* de l'œil suivant les mêmes trois xes, et par là *même* d mettre en rapport ces changements avec les perception d déplacement *enregistrées simultanément* dan les mêmes co ditions dynamiques. La méthod est soumise *dans ses différentes* parties à une évaluation critique

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MARRIAGES BETWEEN THE DEAF AND HEREDITARY DEAFNESS IN FINLAND

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According to the 1950 population census, Finland has 130.7 deaf per 100,000 inhabitants, which must be regarded as quite high figure. A study was conducted in 1961–1965 of marriages between two deaf persons. They totalled 536 in June 1961 and 534 of them were covered by this study. The 534 marriages between deaf partners produced 1126 children, an average of 2.1 per marriage. This is appreciably lower than the general level in the country. Childless marriages accounted for 17 per cent. Of the children born of the marriages, 4.6 per cent were deaf. To establish genetic deafness, a family tree was compiled for each proband in the material. It extended backward to at least the third generation and included the children of the probands. Rosin's statistical method was used to test the genealogical analysis. The genetic analysis revealed that 52 per cent of the isolated cases were genetic.

It is possible under the current law in Finland for two deaf persons to marry without permission of the President of the Republic only if the deafness of at least one of the partners is non-genetic. The practice is thus quite different from that in e.g. the other Nordic countries. More liberal legislation has been deliberated in recent years in Finland and Bill has been introduced to allow two deaf persons to marry freely when no other health obstacles are involved than genetic deafness. As no major study of hereditary deafness has been conducted in Finland, an investigation was required from the legislative standpoint if no other.

A study of the *prevalence of deafness* was published in Finland over fifty years ago (Björkqvist 1916). According to it the number of deaf in 1880–1912 was 11.2–11.6 per 10 000 inhabitants. Information supplied by the Central Statistical Office of Finland from the 1950 population census gave the number of deaf or deaf mute" as 5338. As the population of Finland at the end of 1949/beginning of 1950 was 4,00 ,082, the number of the deaf per 100,000 inhabitants was 130. This is slightly higher than the figures reported by Björkqvist for 1880–1912. According to information received from the Association of the Deaf in Finland there are in our country 4500 deaf persons who have attended a school for the deaf. However persons who only became deaf at a later age must be added to

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social class to which the subjects examined belong. Furthermore the occurrence of isolates and the prevalence of intermarriage may increase the spread of genetic deafness. The level of general public health work has the same influence when the work is more active the proportion of genetic cases elicited grows. Table 2 shows the percentages of persons with hereditary deafness according to different authors. The percentages vary from 4.0 to 78.0 It must be pointed out, further that the percentages of genetic deafness obtained solely through establishing deafness among pupils of a school for the deaf is in most cases not the same as the corresponding proportion for the country as a whole

Purpose of the investigation

The present investigation had three principal aims

(1) To find out how many children are born of marriages between deaf persons and especially how great a proportion of these unions are childless

(2) To establish how great a proportion of the children born of these marriages are deaf

(3) To disco er the incidence of genetic deafness in Finland

MATERIAL AND METHOD

Itinerant preachers function in Finland as special caretakers of the deaf They are State-paid officers who are commissioned to care for all the deaf in their district, including those who do not belong to the Church. From these itinerant preachers lists were obtained of all marriages between two deaf persons For each deaf person, basic information was obtained from the form completed when the subject sought admission to school at the age of 8 The data were supplemented by sending questionnaires to all th deaf in the material Twenty families failed to reply and f r them information was obtained from the church register office After this, there remained only two f milies for which no information was vailable both had moved abroad during the investigation period

The method employed in collecting the materi l for the actual genetic study was the so-called censu method (Akesson, 1961) In accordance with this, all persons fitting a certain formula at a certain point of time were included in the study These were the deaf persons married with one nother in 1961 The personal data of th probands were also examined nd as accurate information as possible was equired concerning their f milies. These data were btained from the archives of the population register Complementary information was obtained from the clergymen for the deaf congregational almoners and social welfare boards. The data were collected partly through questionnaires, partly by the investigator

TABLE 1 *Prevalence of deafness in different countries*

Country	Year of investigation	Number of deaf per 100 000 inhabitants
Belgium	1950	59
Egypt	1937	60
England and Wales	1930	[illegible]
Honduras	1935	138
India	1931	66
Iceland	1948	76
Canada	1911	63
Norway	1930	63
France	1916	47
Scotland	1930	8
United States	1930	46

this total The information given by the Association of the Deaf in Finland thus concurs fairly well with the results of the population census.

The relative number of the deaf varies in different countries. Several international statistics have been published The statistics published in 1953 by the World Health Organization are reproduced in Table 1 Compared with the figures of this table the proportion of deaf in the total population must thus be regarded as fairly high in Finland (130 7 per 100 000 inhabitants)

Data on the number of persons with *genetic deafness* vary greatly This is probably because of the difficulty of defining hereditary deafness without comprehensive genealogical studies, especially when the deaf person is an only child or the only deaf person among a small number of siblings The number of persons with genetic deafness may also be related to the

TABLE 2 *Percentage of genetic deafness according to different investigators*

Author	Year of investigation	Percentage of hereditary deafness
Lindenov	1945	45.5
Gagnon	1961	25.0
Best	1928	4 0
Bordley	1952	1 0
Kinney	1953	11 6
Fowler & Basek	1934	3 7
Zonderman	1959	4 0
Goldstein *et al*	1960	8 1
De Reynier	1939	28.5
Deraemaeker	1960	41.5
Rosin	1963	8 0

social class to which the subjects examined belong Furthermore the occurrence of isolates and the prevalence of intermarriage may increase the spread of genetic deafness The level of general public health work has the same influence when the work is more active the proportion of genetic cases elicited grows. Table 2 shows the percentages of persons with hereditary deafness according to different authors. The percentages vary from 4.0 to 78.0 It must be pointed out, further that the percentages of genetic deafness obtained solely through establishing deafness among pupils of a school for the deaf is in most cases not the same as the corresponding proportion for the country as a whole

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(1) To find out how many children are born of marriages between deaf persons and especially how great a proportion of these unions are childless

(2) To establish how great a proportion of the children born of these marriages are deaf

(3) To discover the incidence of genetic deafness in Finland.

MATERIAL AND METHOD

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The method employed in collecting the material for the actual genetic study was the so-called census method (Åkesson 1961) In accordance with this, all persons fitting certain formula at a certain point of time were included in the study These were the deaf persons married with one another in 1961 The personal data of the probands were also examined and as accurate information as possible was acquired concerning their families. These data were obtained from the archives of the population register Complementary information was obtained from the clergymen for the deaf congregational almoners and social welfare boards. The data were collected partly through questionnaires, partly by the investigator

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Honduras	1935	138
India	1931	66
Iceland	1946	76
Canada	1931	63
Norway	1930	53
France	1946	47
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Deraemaeker	1960	41 5
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TABLE 4 *The order of birth of the deaf child among the siblings*

Ordinal number child	Total of children	Number of deaf	Percentage
1st	1053	270	25.6
2nd	983	226	23.0
3rd	876	156	17.8
4th	732	117	16.0
5th	582	94	16.0
6th	441	53	12 0
7th	314	44	14 0
8th	224	36	16.0
9th	142	37	26.0
10th	76	10	13 0

in the family This could not be elicited in [illegible] cases. Table 3 which includes the probands themselves, gives the t tal of children in the families

Families with 3–5 children account for 41 1 per cent of the total material Only [illegible] 0 per cent of them had a single child, while 3.8 per cent had more than 10 children Table 4 shows the ordinal number of the deaf child in families with 1–10 children.

In the f milies with 1–4 children the deaf were relatively most numerous in those with 1 child and the proportion declined steadily as the number f children in th family increased.

It was impossible to elicit the age [illegible] which the persons in the material became deaf Deafness was established at the age of under 1 year in 485 cases (45 7 per cent) and not until over 5 years in 55 cases (5.2 per cent)

TABLE 5 *Notified cause of deafness*

Cause of deafness	Number	Percentage
Encephalo-meningitis	242	43.8
Scarlet fever	79	14.2
Influenza	76	13.7
Ear diseases	32	5.8
Whooping cough	25	4.5
Cranial-brain injury	19	3.4
Poliomyelitis	18	3.3
Maternal diseases during pregnancy	15	2.7
Birth traumata	14	2.5
Diphteria	7	1.3
Syphilis	7	1.3
Mumps	2	
Variola	2	
Total	558	

visiting about 60 communes to throw light on questions pertaining to the families of the probands.

Selected for the investigation material were all families living in Finland in June 1961 in which both parents were deaf These families totalled 556 but 2 families emigrated in the course of the investigation The final material thus consisted of 554 marriages between two deaf spouses The percentage of marriages between the deaf in Finland that was covered by the investigation was thus 99 6 However as will be seen later sufficient data for the genetic study were not obtained on all of them Of the marriages, 507 were marriages in which both spouses were alive in 47 of them one spouse had died The basic material thus included 1061 persons These persons were born in 1870–1943, and at the time of investigation the majority were 40–60 years of age At the time of the investigation 645 persons (60 8 per cent) were at least 42 years old and the number of children in most of the families can thus be regarded as practically final The number of marriages between the deaf varied greatly in different parts of the country The number was smallest on the southern cost of Finland in the administrative district round Helsinki (12 1 per 100 000 inhabitants) and highest in the administrative district of Vaasa (32 0 per 100 000 inhabitants)

BASIC STUDY

A Probands

Proband in this study denotes deaf persons who intermarried The data in the following thus refer to the conditions in their childhood home

A total of 874 of the persons studied came from farming or worker families the farming families constituted the largest occupational group (49.2 per cent) The mother s age at the time of the child s birth was 21–30 years in over half of the cases (53 4 per cent) and over 40 in only 5 4 per cent The material included only two parturients aged over 45 It is important for the genetic study to know the total number of children

TABLE 3 *Number of the children in the families studied*

Number of children	Number of families	Percentage	Number of children	Number of families	Percentage
1	73	6.9	10	36	3.1
2	107	10 0	11	16	1 5
3	141	13.7	12	13	1.2
4	150	14.3	13	8	0.8
5	141	13.1	14	3	
6	127	12.0	15	—	
7	88	8.3	16	—	
8	84	8 0	17	1	
9	66	6.3			

TABLE 4 *The order of birth of the deaf child among the siblings*

Ordinal number child	Total of children	Number of deaf	Percentage
1st	1053	270	25.6
2nd	983	226	23.0
3rd	876	156	17.8
4th	732	117	16.0
5th	582	94	16.0
6th	441	53	12.0
7th	314	44	14.0
8th	226	36	16.0
9th	142	37	26.0
10th	76	10	13.0

in the family This could not be elicited in 5 cases Table 3, which includes the probands themselves, gives the total of children in the families.

Families with 3–5 children account for 41 1 per cent of the total material Only 6 9 per cent of them had a single child, while 3.8 per cent had more than 10 children Table 4 shows the ordinal number of the deaf child in families with 1–10 children

In the families with 1–4 children the deaf were relatively most numerous in those with 1 child and the proportion declined steadily as the number of children in the family increased

It was impossible to elicit the age at which the persons in the material became deaf Deafness was established at the age of under 1 year in 485 cases (45 7 per cent) and not until over 5 years in 55 cases (5.2 per cent)

TABLE 5 *Notified cause of deafness*

Cause of deafness	Number	Percentage
Encephalo-meningitis	242	43.6
Scarlet fever	79	14.2
Influenza	76	13.7
Ear diseases	32	[illegible]
Whooping cough	25	4.5
Cranial-brain injury	19	3.4
Poliomyelitis	18	3.2
Maternal diseases during pregnancy	15	2.7
Birth traumata	14	2.5
Diphteria	7	1.3
Syphilis	7	1.3
Mumps	2	
Variola	2	
Total	538	

TABLE 6 *Number of deaf siblings*

Number of deaf siblings	Number of families	Percentage
1	98	9.3
2	31	2.9
3	9	0 8
4	10	0 9
5	1	
No other deaf except the proband	912	86 0
Total	1061	

but this figure naturally cannot be regarded as reliable Table 5 shows the notified cause of deafness

The cause of deafness was thus given in 538 cases (50 7 per cent) and was not known in 523 cases (49.3 per cent) The commonest cause of deafness given was encephalo-meningitis, and this is in fact a general finding of studies on the etiology of deafness Scarlet fever was the second most frequent cause of deafness it too is closely associated with ear diseases and is nowadays a fairly rare cause of deafness The third place was taken by influenza, chiefly because of the severe influenza epidemic in Finland after World War I This cause of deafness is closely associated with encephalitis Attention is attracted also by poliomyelitis as a disease causing deafness, for epidemics of poliomyelitis have not been found to cause deafness in Finland since World War II The greater neurotropism of the earlier epidemics obviously explains this difference The number who became deaf through maternal diseases during pregnancy seems rather small This must surely be because these diseases (e g rubella) during pregnancy were not given sufficient thought The share of syphilis also appears too small it is known in fact that an endeavour is always made to conceal this disease Eighty six per cent of the families had only one deaf child (the proband) whereas 14 per cent had a minimum of 2 deaf children

TABLE 7 *Number of children of marriages between deaf persons*

Number of children	Number of families	Percentage	Number of children	Number of families
None	96	17 0	6	9
1	128	23.0	7	4
2	160	29 0	8	4
3	[illegible]	15.0	9	1
4	42	8 0	10	1
5	25	5.0		

TABLE 8. *Number of deaf children of marriages between deaf persons*

Number of deaf children	Number of families
None	521
1	19
2	11
3	2
4	—
5	1

II Marriages between deaf persons

The following data refer to conditions in marriages between two deaf persons. The number of children of these marriages is given in Table 7. The commonest number of children of marriages between deaf partners has thus been 2. There were only 19 (3.4 per cent) families with more than 5 children, 17 per cent had no children at all and most of these stated they had not wanted children. The number of deaf children is shown in Table 8.

Marriages producing one or more deaf children totalled 5.9 per cent. Thirteen of them were marriages in which the family's only child was deaf. On the other hand, a family with 5 deaf children had not a single child capable of hearing. One family had deaf twins.

As [illegible] of the 1126 children from marriages between deaf persons were deaf, the percentage of deaf children was 4.6 per cent.

It was not possible to obtain accurate information about the age of onset of the deafness. But one observation is interesting: there were no definite hearing losses occurring at a later age, though 15.4 per cent of the probands themselves were persons who reported that they had lost their hearing only after the age of 3, and for almost all of them the confirmation of loss of hearing was first made only after reaching the age of 3 years.

The parents were unable in 42 cases to give the cause of the hearing loss, and in these cases the child had in fact always been regarded as congenitally deaf. Encephalo-meningitis was the cause of deafness in 6 cases, and the former had been diagnosed in hospital in all of them. An ear disease was blamed in 2 cases: there is reason to doubt this since no complications were established in either case in connection with otitis media. In one case a severe birth trauma and in another whooping cough was stated to be the cause.

GENETIC STUDY

Methods

For the genetic study of deafness it was necessary to check the material. 3 years had elapsed between the basic study and the start of the genetic study. Hence the material consisted of 562 marriages between

TABLE 6 *Number of deaf siblings*

Number of deaf siblings	Number of families	Percentage
1	98	9.3
2	31	2.0
3	9	0.8
4	10	0 9
5	1	
No other deaf except the proband	912	86 0
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TABLE 7 *Number of children of marriages between deaf persons*

Number of children	Number of families	Percentage	Number of children	Number of families
None	96	17 0	6	0
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2	160	29 0	8	1
3	84	15.0	9	1
4	42	8 0	10	1
5	25	5.0		

TABLE 8 *Number of deaf children of marriages between deaf persons*

Number of deaf children	Number of families
None	521
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2	11
3	2
4	—
5	1

B Ma riages between deaf persons

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TABLE 7 *Number of children of marriages between deaf persons*

Number of children	Number of families	Percentage	Number of children	Number of families
None	90	17.0	6	[illegible]
1	128	23.0	7	1
2	160	20.0	8	1
3	81	15.0	9	1
4	42	8.0	10	1
5	25	5.0		

TABLE 9 *Testing the h value by the Chi test The probable incidenc of exogenous cases e was 0.37*

S	n_s	$E(n(I))$	$O(N(L))$	$O-E$	χ^2
2	97	88.6	91	+2.4	0.60
3	122	102.8	114	+11.2	6.55
4	142	112.2	100	−0.2	2.81
5	116	86.9	88	+1.1	0.01
6	131	91.3	100	+8.7	2.06
7	119	83.2	84	0.8	0.02
8	89	61.1	62	+0.9	0.02
9	80	54.4	55	0.6	0.01
10	40	27.1	25	−2.1	0.31
11	23	22.4	21	−1.4	0.18
12	14	9.[illegible]	7	−2.8	1.38

$\sum (n) = 14.14$
$P < 0.30$

TABLE 10 *Material treated by the Chi test*

		Number of sibling series				
		One deaf		Several deaf		
S		Established	Expected	Established	Expected	χ^2
2	97	91	88.72	6	8.28	0.825
3	122	114	103.33	8	18.63	6.083
4	142	103	112.86	39	29.14	3.337
5	116	88	87.67	28	28.33	0.384
6	131	103	95.30	28	35.70	1.661
7	119	81	81.28	33	31.72	0.226
8	89	82	61.97	27	27.03	0.000
	80	55	55.19	25	24.81	0.009
1	40	25	27.52	15	12.48	0.406
11	33	21	22.75	12	10.25	0.299
12	14	7	9.71	7	4.29	
13	9	8	6.29	1	2.71	
14	6	6	4.23	—	1.77	
15	3	2	2.14	1	0.86	0.032
16	1		0.72	1	0.28	
17		—	—	—	—	
18	1	—	0.71	1	0.26	
19		—	—	—	—	
20	1	1	0.75	—	0.25	
	1004	770				

$\sum (n) = 13.035$
$P < 0.30$

deaf persons and the probands in the genetic study totalled 1194 In 47 families one of the spouses had died before the beginning of the genetic study

To establish genetic deafness, a genealogical tree was drawn for each proband in the material It extended backwards for at least three generations and included the children of the probands The genealogical trees went back temporally to the 18th century However the annotation concerning deafness or other corresponding defects rating from this time are deficient or lacking completely

The heredity of deafness in the family of each proband was assessed from the family trees The district of residence of the deaf person s family *and the prevalence of deafness in the region in question were also con*sidered If a definite area of isolation was involved it was considered to sustain the possibility that deafness is inherited

The statistical method evolved by Rosin (1963) was used in support of the genealogical tree analysis This method is, however applicable only to cases in which both parents of the proband have their hearing and there has been more than one child in the proband s sibling series The part of the material that remained outside the statistical study was so small and heterogeneous that there was no point in analysing it by other statistical methods No reliable results could have been achieved because of the small number of similar cases

The exogenous value h was calculated first by Rosin s statistical method The expected values for the deaf vis à vis the sibling series of the probands in accordance with the Chi test were calculated by means of h The expected values were calculated from the following formula

$$F = n \frac{p_s^{\,s-1}}{(1-q^s)/s + h} + h$$

In addition to the above values e which illustrates the probable prevalence of exogenous cases in the population was calculated from the formula

$$e = \frac{4h}{1+4h}\, m$$

Results

It was seen from the family trees that both parents of 20 probands were deaf and one parent of 13 *probands was deaf It was possible to regard* deafness as recessively inherited in these cases Moreover two cases were established in which recessive deafness had obviously been caused by two different genes independently *definite dominant inheritance was stated* in one case only No sex linked hereditary deafness was encountered

A total of 393 probands (34 8 per cent of the total material) had rela

TABLE 9 *Testing the h value by the Chi test The probable incidence of exogenous cases e was 0.3*

s		$E(n(l))$	$O(N(L))$	$O-E$	χ^2
2	97	88.6	91	+2.4	0.69
3	122	102.8	114	+11.2	6.55
4	142	112.2	103	−9.2	2.84
5	116	86.9	88	+1.1	0.01
6	131	94.3	103	+8.7	2.06
7	119	83.2	[illegible]	+0.8	0.02
8	89	61.1	62	+0.9	0.03
9	80	54.4	55	+0.6	0.01
10	40	27.1	25	−2.1	0.34
11	33	22.4	21	−1.4	0.18
12	14	9.6	7	−2.5	1.38

$\chi^2_{(11)} = 14.11$
$P < 0.30$

TABLE 10 *Material treated by the Chi test*

s		Number of sibling series				χ^2
		One deaf		Several deaf		
		Established	Expected	Established	Expected	
2	97	91	89.72	6	8.28	0.628
3	122	114	103.35	8	16.65	6.082
4	142	103	112.86	30	29.14	3.337
5	116	88	87.67	28	28.33	0.384
6	131	100	93.30	28	35.70	1.661
7	119	81	81.28	38	34.72	0.226
8	89	62	61.97	27	27.03	0.000
9	80	55	56.19	24	24.81	0.000
10	40	25	27.52	1	12.48	0.406
11	33	21	22.75	12	10.25	0.299
12	14	7	9.71	7	4.29	
13	9	8	6.29	1	2.71	
14	6	6	4.27	—	1.77	
15	3	[illegible]	2.14	1	0.86	
16	1	—	0.72	1	0.28	0.032
17	—	—	—	—	—	
18	1	—	0.74	1	0.26	
19	—	—	—	—	—	
20	1	1	0.75	—	0.25	
	1004	770				

$\chi^2_{(10)} = 13.035$
$P < 0.30$

tions who were deaf or hard of hearing In 15 cases the parents of the *proband had been closely related The limit of close kinship in this study* was set at 3 cousinship

The number of probands accepted for statistical analysis was 1004 The cases in which the proband s parents had been deaf and the proband had been the only child were omitted Cases in which the necessary information on the siblings of the proband had not been obtained were also omitted

The exogenous value *h* was 0 148 The fitness of this value was tested by the Chi method and the *P* value obtained was <0 30 The result is given in Table 9

The fitness of the material for the recessive formula of inheritance was tested by the Chi method and the expected values corrected by *h* (Table 10)

The value of *P* at 10 degrees of freedom was 0 30 By Rosin s method, *e* was 0.37 m in the present work *M* represents the incidence of anomaly *in the population There were, thus 37 per cent exogenous cases in the* material In 770 cases the parents of the deaf had been able to hear and the proband was the only deaf sibling The 37 per cent refers to the total of 1004 probands i e the number of exogenous cases is 372 As the above-mentioned isolated cases (the proband the only deaf sibling) was 770 372 cases gives a ratio of 48 per cent in all If we assume that all the cases in which there were other deaf siblings in addition to the proband are genetic we arrive at the finding that 48 per cent are exogenous

DISCUSSION

The sibling series of the probands in the present study was fairly large an average of 6 children *These series have been smaller in other corresponding studies* Rosin (1963) obtained a mean of 5 children in his study of Pfänder s material and the same averages for Stevenson s and Cheeseman s material The largest family sizes in these studies, too, were 12–13 children whereas the largest sibling series in the present study was 20 Comparison of the number of deaf with the number of all siblings in the proband families showed that 23.3 per cent of all the siblings in the study were deaf This concurs with corresponding findings in earlier works

The present material included 26 probands with both parents deaf All the siblings of the probands had also been deaf in these cases Cases in which only one of the proband s parents had been deaf numbered 7 and these families had had a total of 17 children of which 12 were deaf All these cases quite obviously involved recessive deafness

The material included only one definite case of dominant deafness and no sex linked hereditary deafness was established Two cases involved an obvious recessive deafness caused by two different genes

The exogenous value *h* was 0 148 *h* = 0.273 was obtained by Rosin (1963)

from a Swiss material and $h = 0.071$ was established for Northern Ireland. The h value in the present study falls between them The value $e = 0.37$ m in the present study also falls between those reported by Rosin, I.e. $e = 0.32$ m and $e = 0.22$ m

Further comparison of the values revealed that 75 per cent of the isolates in the Swiss material and 48 per cent in the Nothern Irish material were exogenous the latter is the same as the result obtained here.

The application of Rosin s method to the Finnish material involved a few potential errors. Cases in which the sibling series included other deaf besides the proband are assumed to be genetic in this method But in the Finnish material the family size was larger than in the Central European studies. The possibility that as many as 2 children deaf for exogenous reasons might be included in the same sibling series thus grows slightly especially as the public health work in the rural districts was still fairly small at the beginning of the century around the time of birth of the probands Another factor of error is that recessive deafness is caused by at lea t two different genes independently though this cannot be a very great error considered as a whole The finding that a little over a half of the cases were of genetic origin can therefore probably be considered to be correct In Rosin s (1063) study about 00 per cent of the cases in Switzerland and about 78 per cent in Northern Ireland were genetic. In earlier studies Lindenov (1945) established a 45 per cent genetic cases in Denmark DeReynier (1959) for Switzerland, reported 290 per mille ge netic cases and 331 3 per mille undefined congenital cases. In Belgium, Deraemn ker (1960) f und that hereditary cases accounted for 44.5 per cent and Gagnon & Montreuil (1964) established 25 6 per cent hereditary cases in n l stitutionalised material in Canada.

Ratios of deaf persons in the total population show that Finland heads the statistics in Europe with 130 deaf per 100 000 inhabitants, while even for Switzerland the figure is only 91 in 100 000 Björkqvist (1916) provided information on the occurrence of several isolates, and the existence of the same isolates was established in the present work as well This observation together with the great number of the deaf helps to explain the high number of genetic cases

If the deafness of the probands was genetic in 52 per cent, the number (4 6 per cent) of deaf children born of marriages between them appears t be fairly small. But there are many explanations f r this. The law prohibits marriage between two persons with genetic deafness. For this reason most of the marriages wer between a genetically deaf and a non genetically deaf partner In addition, 17 per cent of the marriages were hildles and the parent in these cases almost invariably said that they did not want children as they had been told that it was very possible that their ff pring would be deaf Owing to the sources of error mentioned earlier the proportion of th genetically deaf (2 per cent) cannot be regarded as fully accurate

ZUSAMMENFASSUNG

Nach der im Jahre 1950 durchgeführten Volkszählung gibt es in Finnland auf 100000 Einwohner 130 7 Taube welche Zahl als ausgesprochen hoch angesehen werden muss. In den Jahren 1961–1965 wurde eine Untersuchung über Ehen durchgeführt welche zwischen zwei tauben Personen geschlossen waren Im Juni 1961 gab es 556 solcher Ehen wovon 554 in diese Untersuchung miteinbezogen werden konnten In diesen Ehen wurden 1120 Kinder geboren d h. 2 2 Kinder pro Ehe Diese Zahl war bedeutend niedriger als die Zahl der Kinder pro Ehe im Landesdurchschnitt 17% der Ehen waren kinderlos Von den Kindern der Ehen waren 4 6% taub Um die Erblichkeit der Taubheit nachzuweisen wurde für jeden Probanden ein mindestens drei Generationen umfassender und auch die Kinder des Probanden einschliessender Stammbaum ausgearbeitet Als Grundlage der Stammbaumuntersuchung wurde die von Rosin entwickelte statistische Methode angewandt Mit Hilfe der genetischen Untersuchung konnte festgestellt werden das s von den Einzelfällen 57% genetisch bedingt waren

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THE DEVELOPMENT OF THE STRIA VASCULARIS IN THE MOUSE

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We used the electron microscope to study the evolution of the stria vascularis from a single layer of cuboidal ectodermal cells resting on spiral ligament fibroblasts to a composite epithelium of several layers of three different kinds of cells. In the process, complicated interdigitations form between neighboring cells which greatly increase surface area and would seem to increase fluid transport capacity. The number of microvilli decreases and each marginal cell's kinocilium disappears during the second week after birth. However there is an increase in the number of clear fluid-containing vesicles in the superficial part of the marginal cells.

INTRODUCTION

We were led to study the development of the stria vascularis because of our interest in hereditarily deaf Shaker 1 mice. We have compared the development of the organ of Corti in these mice with normal ones and learned that significant differences appear in the organ of Corti at about the 10th day after birth. Vacuoles form in scattered hair cells and efferent innervation fails to occur (Kikuchi & Hilding, 1965 *b*). Soon afterwards, these animals begin to loose their hearing acuity (Mikaelian & Ruben, 1964). As other authors have suggested, it is possible that a failure in nutrition or oxygenation may account for the maldevelopment of the organ of Corti in these animals. Since the stria vascularis is generally accepted as the source of endolymph and thus of hair cell nutrients it seemed worthwhile to use the electron microscope to study the development of the stria vascularis. A subsequent report will deal with our findings in Shaker 1 mice.

In 1886 Baginsky wrote an excellent description of the important events in the development of the stria vascularis. He showed how the stria of rabbit embryos become thicker because of additional layers of relatively cuboidal cells while the spiral prominence retained only a single layer of epithelium of it. Weibel (1957) used light microscopy to study the stria in mice. He decided that the epithelium of the stria consists of two layers,

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ZUSAMMENFASSUNG

Nach der im Jahre 1950 durchgeführten Volkszählung gibt es in Finnland auf 100000 Einwohner 130 7 Taube welche Zahl als ausgesprochen hoch angesehen werden muss. In den Jahren 1961–1965 wurde eine Untersuchung über Ehen durchgeführt welche zwischen zwei tauben Personen geschlossen waren Im Juni 1961 gab es 550 solcher Ehen wovon 504 in diese Untersuchung miteinbezogen werden konnten In diesen Ehen wurden 1126 Kinder geboren d h. 2,2 Kinder pro Ehe Diese Zahl war bedeutend niedriger als die Zahl der Kinder pro Ehe im Landesdurchschnitt 17% der Ehen waren kinderlos. Von den Kindern der Ehen waren 4 6% taub Um die Erblichkeit der Taubheit nachzuweisen wurde für jeden Proband ein mindestens drei Generationen umfassender und auch die Kinder des Probanden einschliessender Stammbaum ausgearbeitet Als Grundlage der Stammbaumuntersuchung wurde die von Rosin entwickelte statistische Methode angewandt Mit Hilfe der genetischen Untersuchung konnte festgestellt werden dass von den Einzelfällen 57% genetisch bedingt waren.

ACKNOWLEDGMENT

The financial support of the Sigrid Juselius Foundation is gratefully acknowledged

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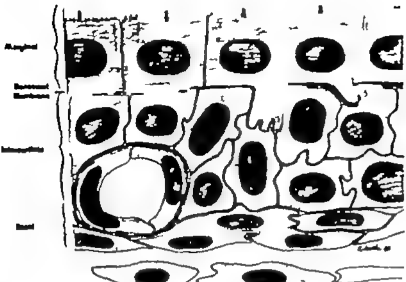

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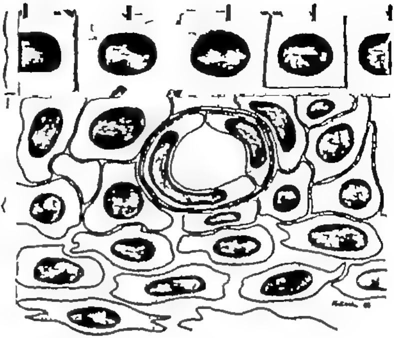
Fig. 2. Stria vascularis of the basal turn of the newborn mouse. This portion of the cochlea develops earlier than the apical turn and three major types of cells can be identified: marginal, intermediate and basal cells. The marginal cells, which are arranged in a single row, face the endolymphatic space. They have dense cytoplasm. At this stage, a few marginal cells have a short process which extends downwards. Microvilli and kinocilia still remain. Remnants of the basement membrane are still visible. A layer of basal cells lies over the connective tissue of the spiral ligament. Intermediate cells are found between the marginal and basal cells. The cytoplasm of intermediate and basal cells is much less dense than that of marginal cells.

The specimens were immersed in cold buffered glutaraldehyde for two hours (Sabatini, Bensch & Barrnett, 1963) and postfixed for one hour in 1 % buffered osmic acid. They were dehydrated in graded alcohol and embedded in Epon plastic. A fine saw mounted in a watchmaker's lathe was used to divide the cochlea through the modiolus and to cut off each turn. Each of the turns was separately remounted on Epon blocks for sectioning. Ultrathin sections were cut on an LKB Ultrotome and examined with an RCA EMU 3G Electron Microscope. Sections were stained by uranyl acetate solution.

FINDINGS

The adult structure of a three layered epithelium is the result of a mixture of a single layer of dark ectodermal cells with subjacent cells derived from the mesodermal tissue of the spiral ligament. As seen in Figures 1, 4 and 5 the newborn stria, of the apical turn consists of a sheet of cuboidal, dark cells. A basement membrane is clearly evident beneath it. This, in turn, rests on fibroblasts of the spiral ligament. The



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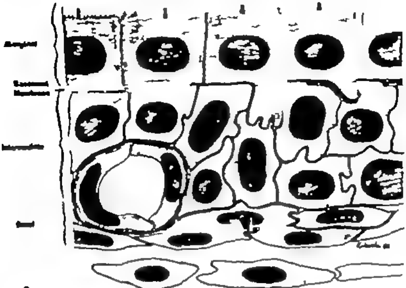
F g 1 St ia asculari f tl e api al turn of the newborn m use In tl is are t t types of cell can be identified an pithelium f marginal cell and fibroblast f the spiral ligament Numerou n icrovilli nd a kinocilium re f u d t the free urf ce of h marginal c ll A ba ement membra e i clearly evident be eatl the m rginal cells The spiral ligament consist of s veral l vers f fibroblasts.

the superficial one derived from ectoderm and the deeper one from mesoderm of the spiral ligament Our findings support this view

The structure of the normal adult stria vascularis has been studied by elec tron microscopy in several species by various including Engström Sjöstrand & Spoendlin (1955) Smith (1957) Chou (1961) Rodrigues Echandia & Burgos (196.) and Hinojosa & Rodriguez Echandia (1966) The epithelium consists of three rather distinct layers of different cell types as they have described The layer bordering endolymph consists of marginal cells which have a dense cytoplasm which explains why they are often called dark cells The layer next to the connective tissue of the spiral ligament is called the basal layer and consists of basal cells Between these two layers is a zone of cells which interdigitate freely with the marginal and basal cells They are called intermediate cells The basal and inter mediate" cells are called light" cells by some authors Figure 3 illustrates these features diagrammatically

MATERIAL AND METHODS

After ether anesthesia normal mice at various stages from newborn to adulthood were decapitated The cochleas were removed and an opening made through the bony walls to permit access of fixative solutions



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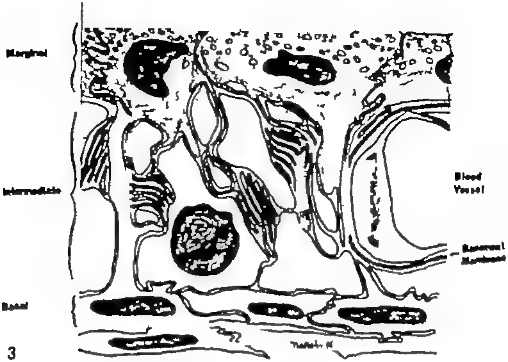

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FIG. 3 Adult stria vascularis. Vesicles are well-developed and distributed between the free surface and the nucleus of the marginal cells. Cytoplasmic folds form a complex pattern. Basement membrane is only observed outside of blood vessels. Basal cells each have a long process which extends upward towards marginal cells.

presence of a basement membrane under the superficial layer strongly supports Weibel's (1957) view that it is the only layer derived from neuroectoderm. Even at birth the development of the stria near the basal end of the cochlea has progressed to a three-layered epithelium and the basement membrane is present only as remnants (Figs. 2 and 6).

Figure 6 is a low power electron micrograph of marginal and intermediate cells from a newborn mouse. The free surface of the marginal cells in contact with endolymph is covered by small finger-like microvilli. As development progresses these become much less numerous (Fig. 7). As illustrated in Figure 8 a single much larger "kinocilium" projects from each newborn marginal cell. The pattern of the cilium and its basal body resembles the motile cilia of the respiratory tract and earns for these hairs the designation "kinocilia" to differentiate them from the non-motile hairs of the hair cells which have been called "stereocilia". In the newborn organ of Corti each hair cell and supporting cell is surmounted by a kinocilium (Kikuchi & Hilding 1965 *a*). The endolymphatic cells of Reissner's membrane *have kinocilia at birth. Therefore* we are quite certain that each cell in contact with endolymph in the immature cochlear duct has one kinocilium. Most of them disappear by the 10th day after birth in mice or about the time hearing acuity develops.

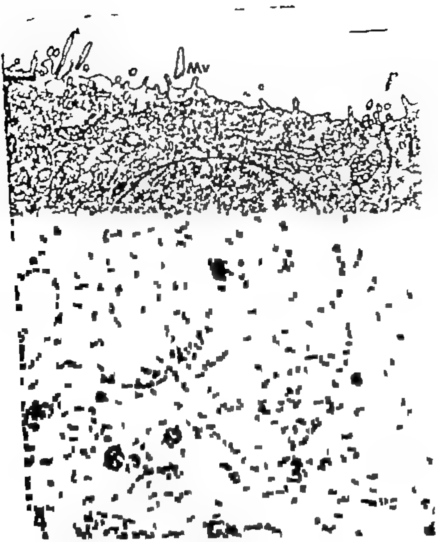

Fig. 4. A low power electron micrograph of marginal cell of the apical turn in the newborn mouse. The cell is roughly cuboidal in shape. Microvilli (Mv) are found at the free surface of the cell. Basement membrane (BM) is evident beneath the cell in this stage. × 20,000.

Numerous small, clear fluid spaces or vesicles are found in mature marginal cells between the nucleus and endolymphatic surface. A few of these are present at birth, as seen in Figure 9, but they increase in size and in number during development (Fig. 7). Occasionally, the endolymphatic cell membrane invaginates to form an "open mouthed" or "pinocytotic" vesicle (Fig. 10). This kind of vesicle is ordinarily regarded as a method that cells use to take in substances from outside (Marchesi & Barrnett, 1964; Nakai, 1965; Lundquist, 1965). In some sections, a hairy layer is seen within the vesicles. We were unable to visualize a mem-

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Fig. 6 M rginal (MC) nd intermedi t cell (IC) from the basal turn of the newborn mouse I the m rgin l cell, few small esicles (V) are present i the part f the cell ne t t the endol mph. A process (P) passes d t the intermediat cell from the cell body. Early formation of complex folds (CF) is seen at the inferior portions of he ll. A erythrocyt (E) is isible insid capillary (C) which i urrounded by basement membrane (BM). Occa ionally the basement m mbrane (rrow) is draw for hort dist nce from the capillary bet een adjacent cells. 88,000

FIG. 5. High power electron micrograph showing basement membrane (*BM*) between marginal (*MC*) and intermediate (*IC*) cells. Mitochondria (*M*), Golgi complex (*GC*) and endoplasmic reticulum (*ER*). [illegible] Apical turn of newborn mouse. × 125 000

brane lining of most vesicles but this may have been due to technical problems.

Another striking change during maturation is an enormous increase in the surface area of each cell due to formation of processes and sheets which fold and interdigitate with neighboring cells. The basal cells become elliptical and each send at least one fold or projection upwards to divide intermediate cells from each other (Figs. 3 and 11). The cytoplasm of intermediate cells and basal cells contains many fewer inclusions than the darker marginal cells, providing a convenient way to distinguish marginal cells from the others. From the simple cuboidal form seen at birth (Fig. 4) in the apical turn the marginal cells interdigitate with adjacent marginal and intermediate cells to form a complex pattern very

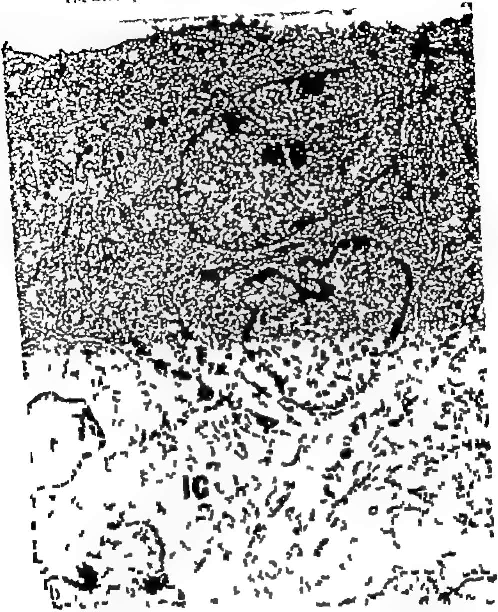

Fig. 4 Marginal (MC) and intermediate cell (IC) from the basal turn of the newborn mouse. In the marginal cell, a few small vesicles (V) are present in the part of the cell next to the endolymph. A process (P) passes down to the intermediate cell from the cell body. Early formation of complex folds (CF) is seen at the inferior portion of the cell. An erythrocyte (E) is visible inside capillary (C) which is surrounded by basement membrane (BM). Occasionally the basement membrane (arrow) is drawn for a short distance from the capillary between adjacent cells. 30,000

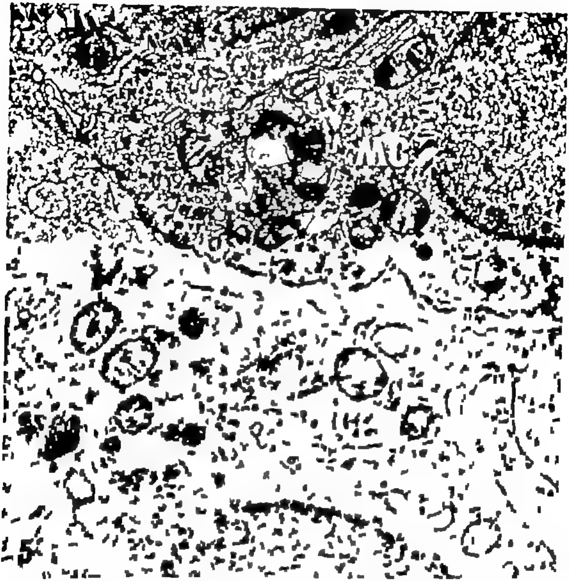

FIG. 5. High power electron micrograph showing basement membrane (BM) between marginal (MC) and intermediate (IC) cells. Mitochondria (M), a Golgi complex (GC) and endoplasmic reticulum (ER) are found. Apical turn of newborn mouse. ×25 000

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FIG. 7 Low power electron micrograph of the adult mouse stri ascularis Duri g maturati n, microvilli become les numerou nd the free surface f the margi al cell becomes smooth The cyt plasm of the marginal cell next to the end lymphatic space is filled with numerou el ar vesicles (1) Th re is a striking increase f cell urf ce area bec use of f ldi g of thin sheet projecting and interlocking with neighboring cells. The compli ted pattern forms between adjacent intermediat and marginal cells. × 10 000

similar to salivary gland and renal epithelia During the formation of these folds the basement membrane between marginal cells and intermediate cells disappears The only basement membrane in this region is seen surrounding capillaries Sometimes it is drawn for a short distance away from the vessel between neighboring cells

DISCUSSION

The cuboidal cells of the adult spiral prominence rest on a typical basement membrane In this regard they resemble most other kinds of epithelial structures Whether one looks at the tracheal lining oral mucous membrane pancreatic ducts or skin there is a homogeneous acellular

Fig. 8. A kinocilium (K) project from the free surface of ach marginal cell in the newborn stria vascularis. It plays an unknow rol ad disappears by the tenth day fter birth. 134,000.

layer about 200 Å thick separated from the plasma membrane of the epithelial cells by a space about 250 Å wide. This layer forms between the lower urf ce of the epithelium and the underlying connective tissue. However the adult stria vascularis is an exception. No basement mem brane separates the three layers of the strial epithelium from the spiral ligament. We looked for a stage of development where basement mem brane exists. Thi search was timulated by a question of Engstr m. Sjöstrand & Spoendlin (1935) and by Weibel's contention (1957) that only the ingle layer of cells nearest the endolymph were ectodermal. We reasoned that at some stage these cells would have a basment membrane beneath if they were a separate layer derived from the neuro-ectoderm. However if all three layers form by means of multiplication of ectodermal cell origin lly from a single layer one would expect that the basement membrane would be found beneath all three layers. In newborn animals we found a di tinct basement membrane under the dark cell layer (Figs. 4 and 5) lending upport to the concept that only this was ectodermal. Dur ing dev lopment the marginal cells and the cells below become folded together nd the basement membrane is lost. Probably the various kinds

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FIG. 8 A kinocilium (K) projects from the free surface f each marginal cell in the newborn stria ascularis. It plays unknow rol nd disappears by the t nth day after birth. 144,000

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FIG. 9. A high power electron micrograph from the endolymphatic portion of a newborn mouse marginal cell. Mitochondria (M), Golgi complex (GC), endoplasmic reticulum (ER) and ribosomes (R) are distributed throughout the cytoplasm. Vesicles (V) of varying size are concentrated in the endolymphatic surface. × 125,000.

of cells form a composite tissue with only a single basic function but it is interesting to speculate about the possible reason for its development from two germ layers.

The abundant cytoplasmic folds and interdigitations between neighboring cells which form during development have been well-described in the adult form by other electron microscopic studies including Engström, Sjöstrand & Spoendlin (1955), Smith (1957), Yamamoto & Nakai (1964), Rodrigues Echandia & Burgos (1965) and Hinojosa & Rodriguez Echandia (1966). By ten days after birth the adult pattern is reached. As the above authors have stressed, this kind of folding is characteristic of cells engaged in fluid transport.

Another feature of the adult stria which one would expect in cells secreting or absorbing fluid is the presence of numerous vesicles. In the adult the cytoplasm between the nucleus and endolymphatic surface of the marginal cells is filled with numerous vesicles of varying size. At birth there are only a few vesicles, but during development they become more numerous and larger. Many of them become larger than pinocytotic

Fig. 10. A open-mouthed or pinocytotic vesicle at the free surface of marginal cell from an adult mouse. 120,000

vesicles of other cell-types. Infolding of the outer cell surface to form in aginated open mouthed pinocytotic vesicles are not commonly seen. The hazy lining which is seen in some pinocytotic vesicles is a feature of som of the vesicles at each stage after birth. Although some recent studies have related open mouthed vesicles to the discharge of material from within the cell mo t pinocytotic vesicle are associated with uptake of material from the cells surroundings. From its appearance alone we are unable to judge whether the stria is engaged in secretion alone or if it lso has importance in fluid absorption. The marginal cell vesicles could co ceivably be part of either kind of system.

Another daptation commonly found in cell transporting fluids is the f rmation of microvilli. We found that they becom less numerous during dev lopment. The immature marginal cells have a large number of microvilli on their endolymphatic surface, but during maturation they disappear. W found a similar change in the supporting cells of the organ of Corti (Kikuchi & Hilding, 1965) and have not yet arrived at a resonable ex planation.

Each of the cell facing the cochlear duct is surmounted by a single kinocilium at birth. They persist in vestibular sensory epithelia but disappear for some obscure reason in the other kinds of cells. The mar ginal ells lose their kinocilia t about the 10th day or at the same time that hearing begins.

Misrahy Shinabarger & Arn ld (1958) measured the oxygen gradient f om the spiral ligament through the stria vascularis and endolymph to the organ f Corti. Although some might quibbl with their method their result showed that oxygen is supplied to the organ of Corti via the endolymph. The gradient between tria nd endolymph supported the concept that endolymph is formed by the stria. The stria has been regarded by most a the source of end lymph since Shambaugh s meticulous discussion in 1908. Guild (1927) von Fieandt & Saxén (1936) Saxén (1951) and

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from the perilymph, and that it is absorbed by the stria vascularis. Surprisingly studies with radioactive substances have supported this unconventional concept Rauch & Köstlin (1962) Rauch (1963) and Rauch Schnieder & Schindler (1963) used radioactive isotopes of sodium and potassium and found that after injection of labeled KCl into the scala vestibuli it appeared rapidly in the endolymph and also in the stria vascularis. It seems clear from the experiments of Lawrence Wolsk & Litten (1961) and Lawrence (1965) that whatever may be the source of endolymph most of it is probably absorbed near its source and there is little flow of endolymph in a longitudinal pathway Our studies of the various kinds of cells of the cochlear duct during development have convinced us that the epithelium of the stria vascularis is morphologically equipped for fluid transport better than any other type of cochlear tissue The spiral prominence is complicated and could absorb or secrete fluid also The connective tissue beneath the epithelium of the spiral prominence can be subdivided into a portion which probably contains perilymph and another which could be infiltrated by endolymph Hilding (1965) described a cell containing large inclusion bodies which stain with dichromate suggesting that they contain catechol amine which are found in the boundary region between the two connective tissue layers We have found no evidence during this study which would help decide whether the stria is primarily concerned with secretion or with absorption

SUMMARY AND CONCLUSIONS

Electron microscopic observations were made of the stria vascularis in mice at various stages during its development after birth We learned that

At birth the layer of cell next to endolymph, the "marginal or dark" cells, are separated from the cells beneath by a distinct basement membrane Later the basement membrane disappears as the mesodermal cells beneath begin to interdigitate with the marginal cells. This finding strongly supports Weibel's theory that the marginal cells are the only layer of the epithelium of the stria vascularis that is derived from neuro-ectoderm.

During maturation cytoplasmic folds and vesicles form producing a pattern consistent with the supposed role of the stria vascularis in fluid transport. At birth the cells of the future stria, at least in the apical part of the cochlea, are cuboidal with little specialization in structure

Numerous microvilli and a single kinocilium are present on the endoplasmic surface of the marginal cells in the immature animals, but these disappear during maturation The kinocilia, like those of the organ of Corti, are lost by the 10th day the stage when hearing begins.

FIG. 11. Each basal cell has long processes which extend upward toward the marginal cells. Adult mouse ×20,000.

Seymour (1954) used histological techniques and came to the same conclusion. Rüedi (1951) doubted that the stria has a secretory function and suggested that its principal role was to absorb endolymph. Naftalin & Harrison (1958) concluded from biochemical considerations that endolymph is produced by a filtration process through Reissner's membrane

from the perilymph, and that it is absorbed by the stria vascularis. Surprisingly studies with radioactive substances have supported this unconventional concept. Rauch & Köstlin (1962) Rauch (1963) and Rauch, Schnieder & Schindler (1963) used radioactive isotopes of sodium and potassium and found that after injection of labeled KCl into the scala vestibuli it appeared rapidly in the endolymph and also in the stria vascularis. It seems clear from the experiments of Lawrence Wolsk & Litten (1961) and Lawrence (1965) that whatever may be the source of endolymph most of it is probably absorbed near its source and there is little flow of endolymph in a longitudinal pathway Our studies of the various kinds of cells of the cochlear duct during development have convinced us that the epithelium of the stria vascularis is morphologically equipped for fluid transport better than any other type of cochlear tissue The spiral prominence is complicated and could absorb or secrete fluid also. The connective tissue beneath the epithelium of the spiral prominence can be subdivided into a portion which probably contains perilymph and another which could be infiltrated by endolymph. Hilding (1965) described a cell containing large inclusion bodies which stain with dichromate suggesting that they contain catechol amine which are found in the boundary region between the two connective tissue layers. We have found no evidence during this study which would help decide whether the stria is primarily concerned with secretion or with absorption.

SUMMARY AND CONCLUSIONS

Electron microscopic observations were made of the stria vascularis in mice at various stages during its development after birth. We learned that

At birth th layer of cells next to endolymph, the marginal or "dark cells, are separated from the cells beneath by a distinct basement membrane. Later the basement membrane disappears as the mesodermal cells beneath begin to interdigitate with the marginal cells. This finding strongly supports Weibel s theory that th marginal cells are the only layer of the epithelium of the stria vascularis that is derived from neuro-ectoderm.

During maturation cytoplasmic folds and vesicles form producing a pattern consistent with the supposed role of the stria vascularis in fluid transport. At birth the cells of the future stria, at least in the apical part of the cochlea, are cuboidal with little specializati n in structure

Numerous microvilli nd a single kinocilium are present on th endoplasmic surface of the marginal cells in the immature animals, but these disappear during maturation. The kinocilia, like those of the organ of Corti, are lost by the 10th day the stage when hearing begins.

ZUSAMMENFASSUNG

Die Entwicklung der Stria vascularis wurde mit Elektronenmikroskopie studiert In der spitzen Windung der neugeborenen Maus findet sich an der Unterseite der oberflächlichen Zellen eine Linie Basalmembrane Nach diesem Befund müssen wir schliessen dass sich die oberflächlichen Zellen aus einer epithelialen Schicht aufbauen Die Säume osmiophilische Strukturen fingerförmige Fortsätze Kinocilia und Microvilli der Stria wurden bei Geburt sichtbar Die Bedeutung der Resultate wird diskutiert

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VESTIBULAR DAMAGE IN STAPEDECTOMY

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Caloric examination of the vestibule is carried out among 90 patients with 108 stapedectomized ears. In 6 patients, examined not less than 6 weeks post-operatively, paresis was found. In one of these patients a progressive course to paralysis was demonstrated almost 2 years after operation. Virtually no association between cochlear and vestibular damage is shown.

Stapedectomy is the method of operation which, as regards hearing, gives the best results in otosclerosis (Schuknecht, McGee & Colman 1960, Gundersen 1963, Meltzer 1963), but experience shows that the inner ear may be damaged by this operation. Shambaugh (1963) points out that the labyrinth is in far more danger from this operation than from stapediolysis. Fussing & Pettersen (1965) found permanent vestibular damage in 12% of patients after stapedectomy as against 3% after stapediolysis.

As with other operations on the labyrinth, a serous or purulent labyrinthitis may arise after stapedectomy. Serous labyrinthitis following stapedectomy may be due to the production of toxic substances by necrosis of fat or the vein transplant (Colman 1962). Other probable causes of labyrinthine damage are loss of a large amount of perilymph and surgical trauma in the form of drilling, strong suction and manipulation of the footplate (Schuknecht, McGee & Colman 1960, Shambaugh 1963, Shea, 1963). Furthermore, direct instrumental damage to that part of the labyrinth lying nearest to the oval window may occur, the otolith organs being primarily affected. A small haemorrhage into the perilymph is probably not harmful (Colman 1962, Gundersen 1963), but an association has been found between large haemorrhage and cochlear damage (Shea 1963). It has not been made clear how much this is due to the fact that the mixing of blood in the perilymph is directly harmful. Particles of bone in the vestibule can give rise to mechanical irritation if they are relatively large (Spector 1961). It has been shown in cats that particles of fat in the vestibule can also be harmful in that they produce considerable fibrosis to the otolith organs (Hayden & McGee 1965).

Damage to the inner ear may include the entire labyrinth or parts of it. Cochlear damage reveals itself either as a high tone deafness, which may

TABLE 1 *Age grouping*

0–19 years	20–39	40–59	60–79	80–
1	12	59	23	1

be progressive (Shea, 1963) or as more general serious affection of the cochlea, occurring in about 2% after total stapedectomy

Colman (1962) states that the semicircular ducts are more resistant to damage than the cochlea. After stapedectomy in cats he found no or only minor histological changes in the vestibular portion, even in cases with severe cochlear damage However clinical reports have been forthcoming which point out the danger of vestibular damage. Stroud (1963) discusses 5 patients with permanent disturbance of balance after stapedectomy and in pre- and post-operative caloric tests in 100 patients, paresis was found in as many as 22% Ali & Groves (1964) and Fussing & Peitersen (1965) found permanent vestibular damage in respectively 10% and 12% of patients.

CASE MATERIAL AND METHOD OF PROCEDURE

The case material consists of 96 patients among whom 108 stapedectomies were performed by the Schuknecht method They are a random sample of almost 500 patients operated in the Ear Nose and Throat department, Haukeland Hospital, since 1961 Ninety five patients suffered from otosclerosis, and a child was operated because of fracture of the stapes. Division into age groups and the degree of otosclerosis may be seen from Tables 1 and 2.

All the patients are investigated using Fitzgerald and Hallpike s caloric test (Fitzgerald & Hallpike, 1942) The method has been somewhat modified in that a time of exposure of 20 sec was used corresponding to about 125 ml water Nystagmus was observed under Bartels spectacles. Permanently set-up apparatus regulated by thermostat was used.

Paresis was reckoned to be present with an average difference of 30 C and 44 C in more than 40 sec. Twenty-three patients are investigated on the stapedectomized side alone on account of fenestration previously carried out elsewhere, chronic otitis with perforation or imminent stapedectomy on the opposite side. In these cases reactions in less than 80 sec are reckoned as pareses.

TABLE 2 *Average hearing loss for frequencies of 500–1000 and 200 cps*

Hearing loss	< 30 dB	30–45 dB	> 45 dB
No. of ears	0	12	48

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Table 2. *Average hearing loss fo frequencies of 500–1000 and 200 cps*

Hearing loss	< 30 dB	30–45 dB	> 45 dB
No. of ears	0	12	46

TABLE 3 *Spontaneous nystagmus post-operatively*

Grade of nystagmus	1	2	3	None	Unknown
Towards the op. ear	2	3	1	99	2
Away from the op. ear	1	0	0		

RESULTS

Impaired caloric response was found in 6 patients in the age group 64–78 years all having pre-operative hearing worse than 45 in the speaking frequency range During the first investigation carried out not earlier than 6 weeks post-operatively paresis was found in these 6 patients A control of one patient 5 months later revealed paralysis The result as regards hearing was good in all cases apart from one patient who had acquired a high tone loss of 20–30 dB at 4000 cps Two patients will be discussed in more detail

Male 66 years Stapedectomized on the right side April 1964 and on the left side May 1965 The operations were not remarkable After the first operation unsteadiness during physical exertion on some occasions after the last attacks of vertigo on moving the head especially to the left Investigation June 1965 revealed paresis on the left side and a control 2 months later showed increased paresis with abolished response at 44 C. Positional nystagmus to the left was found mainly rotatory easily reproducible and accompanied by strong nausea and dizziness.

Female 64 years Stapedectomized on the left side July 1963 and on the right side Nov 1964 Nothing remarkable about the operations Caloric testing in Feb 1965 showed minor paresis on the right side No vestibular symptoms until April 1965 when vertigo unsteadiness and nausea appeared rather suddenly without any hearing phenomena The complaints persisted and repeat investigation in Sept revealed paralysis on the right side unsteady gait and a slightly positive compass gait test

Regarding the 4 other patients, 2 had slight nystagmus towards the operated side in the immediate post-operative days

In 5 patients directional preponderance was found but in 3 of them towards the operated side Paresis of unknown cause was found in the unoperated ears of 2 other patients

The frequency of spontaneous nystagmus during the first post-operative days is shown in Table 3

Among the 108 ears which were examined deafness occurred in 1 after suddenly diminishing hearing and severe vertigo 8 weeks post-operatively without apparent cause High tone loss with reduction at 4000 cps of approx 25–30 dB occurred in 5 ears In a few other patients smaller reductions, mainly at 4000 cps, were found In all patients with diminished

cochlear function, a normal caloric response was found apart from paresis in one with high tone loss.

DISCUSSION

The starting point for our investigation are clinical reports showing that permanent vestibular damage may occur without cochlear damage, and much more commonly After the investigation of Ali & Groves (1964) an impression is gained of a severe vestibular reaction during the im mediate post-operative days. Among 56 patients, 50 had spontaneous nystagmus, 16 of whom had grade 111 and in 7 of these the nystagmus was towards the unoperated side. According to Stroud (1963) patients with diminished caloric function had, as a rule, the most stormy post-operative reaction.

Using the above-mentioned criteria for canal paresis, a relatively small degree of vestibular damage has been found, scarcely 6% This is supported by the very low frequency of spontaneous nystagmus post operatively and to a certain degree also by the relatively low frequency of serious cochlear damage, that is, less than 1%

In the publications mentioned it is not stated which criteria for canal paresis have been used. We have reckoned asymmetries of over 40 sec as paresis, which seems to be the usual figure taken when a limit must be set. However it should be noticed that Fitzgerald & Hallpike (1942) and Thomsen (1953) when investigating normal individuals, did not find greater asymmetries than 20–25 sec. In patients in whom one could not compare results with those from an unoperated ear a lower limit of 80 sec has been used in accordance with several investigations on the normal ear (Fitzgerald & Hallpike, 1942 Hallpike, Harrison & Slater 1951 Thomsen, 1953) A response of this length, nevertheless, can be paretic in that pre-operatively it may have been in the upper limits of the normal range f variation. If a pre-operativ examination had been carried out, further paresis may thereby have been revealed among the 23 unilaterally examined patients. On the other hand, it is not known to what extent the 6 paresis discussed were really due to the stapedectomy operation, especially as paresis was found in 2 patients in the unoperated ear

The cause of differences between materials of stapedectomy in regard to direct vestibular reaction and permanent disturbance must firstly be looked for in the different degree of labyrinthine trauma during the operation It is lso probable that there is a certain difference between the material concerning th degree of otosclerosis and the numbe of previous operations n the labyrinth, which are known to increase the danger of complication

Our 6 patients with diminished response were all above the average age. Thi may be a coincidence, considering that such an association has not been revealed in the other investigations. At all events, operation on the

second ear requires greater precaution in the case of elderly patients. They are more dependent on an intact peripheral vestibular apparatus because the senses of sight and proprioception both of which are important in maintaining balance are often diminished

ZUSAMMENFASSUNG

Kalorische Vestibularisuntersuchungen sind bei 95 Patienten mit 108 stapedektomierten Ohren unternommen worden Bei 6 Ohren die nicht früher als 6 Wochen nach der Operation untersucht wurden sind Paresen gefunden worden Eine von diesen entwickelte sich beinahe 2 Jahre nach der Operation zur Paralyse Es wurde sozusagen kein Zusammenhang zwischen Cochlea- und Vestibularisschaden gefunden

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MODIFICATION OF VESTIBULAR RESPONSES AS A FUNCTION OF RATE OF ROTATION ABOUT AN EARTH HORIZONTAL AXIS

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Eight men completed an experiment in which they were rotated about an Earth-horizontal axis at velocities of 10 and 30 rpm. Both nystagmus and subjective estimates of body position in space were modified by the higher rate of rotation. Subjects who gave essentially veridical estimates of body position at 10 rpm became disoriented at 30 rpm and gave responses closely resembling those of subjects with labyrinthine dysfunction. Subjects who produced sustained unidirectional horizontal nystagmus during constant velocity rotation at 10 rpm produced a reversing horizontal nystagmus during comparable intervals of rotation at 30 rpm. Nystagmus slow phase velocity for both 10 and 30 rpm exhibited a cyclic modulation which was related to orientation relative to gravity. As in previous studies, sickness was produced by rotation about a horizontal axis, and a relationship between mental task and incidence of sickness was again noted.

INTRODUCTION

It has recently been demonstrated (Benson & Bodin, 1966; Correia & Guedry 1964; Guedry 1965) that rotation of a subject about an Earth-horizontal axis produces responses which differ in several respects from those obtained for equivalent rotation about an Earth-vertical axis. Responses during horizontal-axis rotation may be summarized as follows: During constant velocity rotation for periods up to five minutes at certain velocities, rotation is perceived continuously and unidirectional horizontal nystagmus persists throughout the rotation period. Following deceleration from constant velocity rotation the expected experience of postural counter-rotation is either absent or greatly reduced and postrotational horizontal nystagmus is significantly attenuated.

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Opinions or conclusions contained in this report are those of the authors. They are not to be construed as necessarily reflecting the view or the endorsement of the Navy Department.

During constant velocity rotation when the axis of rotation and the longitudinal body axis are horizontal a subject is continuously reoriented relative to gravity During comparable rotation with *the axes vertical*, the subject maintains a constant orientation relative to gravity Hence although equivalent angular acceleration can be imparted to the horizontal semi circular canals in attaining constant velocity in these two situations, only horizontal axis rotation involves continuous reorientation of the vestibular structures relative to gravity

The receptors relevant to the effects associated with horizontal axis rotation have been the *subject of some speculation Benson & Bodin (1966)* have suggested semicircular canal involvement and explain the unique responses during horizontal axis rotation by a traveling deformation of the membranous canals due to the action of gravity on the endolymph filled membranous ducts which have slightly different specific gravity than the surrounding perilymph *Guedry (1965)* and Guedry & Harris (1963) on the other hand, has suggested that nystagmus may be produced when the *otolith structures are stimulated by a change in linear acceleration*, in this case by a change in orientation relative to gravity

The present experiment was conducted to extend observations of the evoked responses to horizontal axis rotation over a wider stimulus spectrum

PROCEDURE

Subjects

Twenty men, officer and cadet flight candidates in the Naval Aviation Training Program, participated in this experiment These subjects had passed recent flight physical examinations and had no apparent symptoms of vestibular disorder *Of these twenty subjects, only eight were able to* complete the experimental sequence The remainder either requested to withdraw or were stopped due to sickness

Apparatus

The apparatus used was the Human Disorientation Device (HDD) and its *bioinstrumentation* (Hixson & Niven 1963) Within the HDD was a chair prepositioned so that the longitudinal body axis was aligned with the axis of rotation which in turn was horizontal The chair was enclosed within a nearly spherical light tight capsule During rotation each subject was fastened to the rotating device by a head and body harness to minimize head or body motions relative to the rotating frame Corneo-retinal potentials were amplified and filtered by a system with an upper cutoff of 25 cps and a time constant of 1.5 sec. A sinusoid potentiometer was used to record instantaneous orientation of the subject relative to gravity and a switch permitted subjects to signal estimates of body

position. Signals were passed through sliprings to an eight-channel Sanborn recorder

Method

Each of the eight subjects who completed this experiment was exposed to four rotation trials, two trials at 10 rpm and two trials at 30 rpm. For each velocity one rotation trial was in a clockwise direction, CW (to the subject's right) and one rotation trial was counterclockwise, CCW (to the subject's left) Order of presentation of velocity magnitude and direction of rotation was counterbalanced over subjects In each trial, the subject was accelerated at 20 /sec² to either 10 or 30 rpm, maintained at that velocity for 120 seconds, then decelerated at 20 /sec² to a stop

Horizontal and vertical components of eye movements were recorded during the entire rotation period. Also, prior to the test runs on four of the subjects, eye movements were recorded while the subject was slowly rotated through 360 degrees as a check for positional and spontaneous nystagmus. Of the eight subjects who completed the experiment, four were asked to signal by pressing a key when they passed through the nose-up and the nose-down positions the other four subjects were required to perform mental arithmetic during rotation. Following completion of each trial, subjects were asked to describe body motions they had experienced during rotation All runs were performed in darkness with each subject instructed to keep his eyes open and to stare "dead ahead"

RESULTS

Nystagmus

Time course of response

Presented in Fig 1 are recordings of horizontal nystagmus obtained from the same subject during comparable time intervals following the onset of angular acceleration for CW horizontal-axis rotational velocities of 10 and 30 rpm It may be observed that throughout rotation at 10 rpm, nystagmus was unidirectional, the direction being that of the response initiated by the angular acceleration. For 30 rpm, nystagmus became bidirectional, i.e *reversing in direction* during constant angular velocity

To compare the average time course of the nystagmus in terms of magnitude and direction for 10 and 30 rpm the velocity of the slow phase of each nystagmic beat for each subject was measured for 120 seconds following the onset of angular acceleration. During some one-second intervals, since nystagmus reversed, the slow phase of the nystagmus was in different directions hence, the mean slow phase velocities for each direction were obtained separately Mean plots for the 10 and 30 rpm CW rotations are presented at the top of Fig. 2 mean plots for the 10 and 30 rpm CCW rotations are at the bottom of Fig 2 Each point in Fig 2 is based on eight subjects.

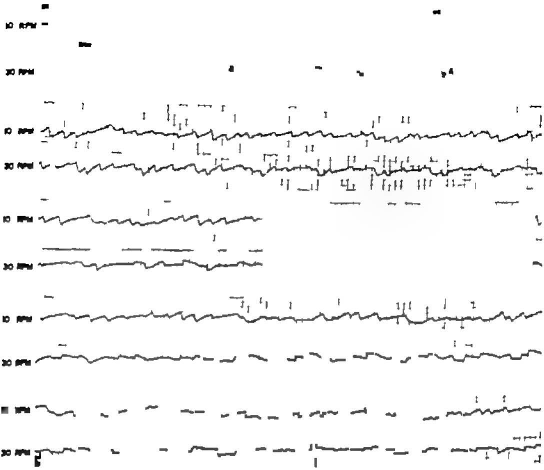


FIG 1 Recordings f horizontal ny tagmus produced by the same subject during comparabl int rvals of clockwise horizontal axis rotation at velocities of 10 and 30 rpm.

From Fig 2 it is obvious that 10 rpm and 30 rpm produced different responses

During angular acceleration to 10 rpm and a short time thereafter the nystagmus magnitude[1] and direction corresponded approximately to the classical response observed during and following angular acceleration about an Earth vertical axis However nystagmus did not return to zero baseline but remained unidirectional throughout rotation with its magnitude oscillating cyclicly but never reaching the zero baseline

Exceptions were noted for two of the eight subjects These two subjects produced a reversing nystagmus during constant angular velocity for one direction of rotation at 10 rpm Examination of eye movement recordings obtained under static conditions revealed that both of these subjects had a spontaneous nystagmus When rotation was of a direction to augment the

[1] Nystagmus att ins cyclic peaks which exceed the magnitud f ny t gm produced by vertical-axl stimulation Thi was st bli hed by comparing responses produced by identical angular acceleration in vertical a d h riz ntal xi stimulu co figurations. Eight men not included in th main xperiment served a sul ject a gular accelerati was 20 /sec² to a rotational velocity of 10 rpm

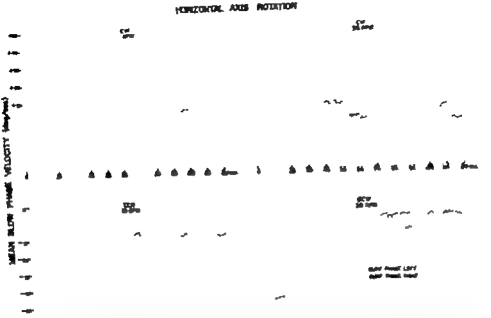


Fig. 2. Plot of magnitude and direction of mean slow phase eye velocity during clockwise and counterclockwise horizontal-axis rotations at 10 and 30 rpm. Note that eye velocity is bidirectional for 30 rpm and essentially unidirectional for 10 rpm. For 10 rpm, negative eye velocities for CW rotation and positive eye velocities for CCW rotation were based on single subjects who had reversing nystagmus at 10 rpm.

spontaneous nystagmus, the response remained unidirectional throughout the rotation period. When rotation was of opposite direction, the subjects produced a reversing nystagmus after 20–30 sec of constant angular velocity. The points across the baseline from the preponderance of points plotted in the 10 rpm trials of Fig. 2 were contributed almost exclusively by these two subjects.

For 30 rpm, the response to angular acceleration was similar to that produced at 10 rpm but it was greater in magnitude due to the greater acceleration × time product. However, whereas the 10 rpm response generally did not return to zero baseline, the 30 rpm response returned to zero baseline within 60 sec from onset of angular acceleration. Seven of the eight subjects produced a definite reversing nystagmus within 60 sec at 30 rpm. One subject produced a unidirectional response throughout both the 10 and 30 rpm trials. The nature of the reversing nystagmus was such that the magnitude oscillated sinusoidally and decayed until the nystagmus was of about equal magnitude in either direction about zero velocity at 60 sec. Since nystagmus was averaged by one-sec time intervals rather than at particular points in the rotation cycle, the modulation of nystagmus is somewhat obscured by the graphic presentation of Fig. 2, but the time course of nystagmus independent of cyclic modulation is apparent.

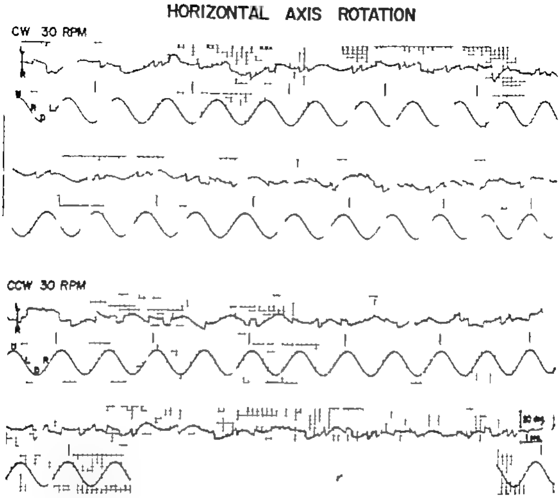


Fig 3 Recording illustrating the relationship of magnitude and direction of horizontal nystagmus to orientation of subject

Relationship of direction and magnitude of nystagmus to body orientation

The relationship of direction and magnitude of slow phase velocity of nystagmus to body position relative to gravity was examined by comparing the nystagmus response to the sinusoid potentiometer recording as shown in Fig 3 The potentiometer recording, while describing body orientation may also be interpreted as a representation of the component of the gravitational linear acceleration vector acting along the horizontal head axes at any given time For example, as illustrated in Fig 4 when the subject was in a nose-up position (0°) or nose-down position (180°) the gravity component would be maximum along the front back head axis ($+x$ $-x$ axis) and minimum along the left–right ($+y$ $-y$ axis) When the subject was in nose-right or nose-left position the component would be maximum along the y head axis and minimum along the x head axis The directions of the linear acceleration vector relative to the head axes are summarized in Fig 4 and it should be noted that when rotation is CW

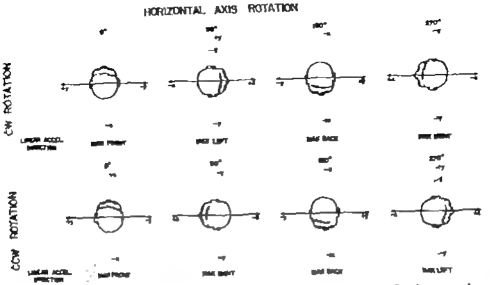


FIG. 4 Direction of gravitational acceleration vector (g) relati t head for f ur angular displacements during one cycle f horizontal xis rotation.

the 90 *position* is equivalent to the 270 *position* when rotation is CCW During CW rotation, 90 position is attained after a 90 angular displacement, whereas during CCW rotation, an angular displacement of 270 from 0 position is required to reach the 90 position.

The cyclic relationship between magnitude and direction of nystagmus and direction of linear acceleration (gravity) is illustrated in the polar plots of mean nystagmus magnitude presented in Fig. 5 The reversing nystagmus generated during 30 rpm was modulated so that fast phase right (nystagmus right) occurred when the linear acceleration (g) was directed to the subject s right nystagmus left was keyed to linear accelera ti n (g) directed left zero eye velocity occurred just after the 0 and 180 positions. Ev n for the sustained unidirectional nystagmus, generated during 10 rpm, magnitude was cyclicly modulated in that maximum slow phase velocity occurred between displacements of 180 –270 and minimum slow phase velocity occurred between displacements of 0 –90 This was true for either rotation direction (CW or CCW) if the *displacements* are defined as in Fig. 4

Each point in Fig 5 is the mean instantaneous slow phase eye velocity for seven ubjects averaged over two cycles of rotation and plotted at 30 intervals.

The exact points of maximum and minimum response for both 10 and 30 rpm varied among subjects, within a range of 40 but generally for

tt 10 rpm, the reversing nystagmus responses from subjects with spontaneous nystagmus ere not included, nd at 30 rpm, the subject with continuou ystagmu was not included.

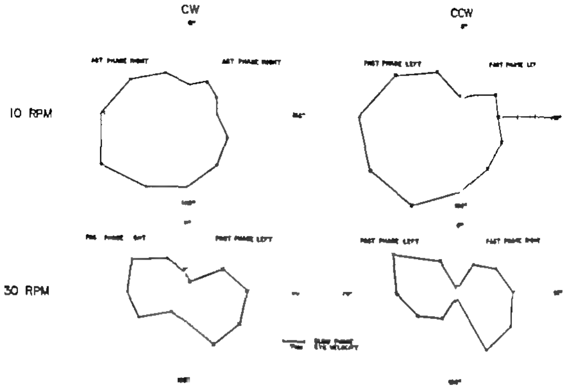


FIG 5 Polar coordinate plots of mean slow phase eye velocity for CW and CCW rotations at 10 and 30 rpm during a given cycle Points are based on 2 cycl s for 7 subjects.

30 rpm maximum nystagmus left lagged maximum linear acceleration left maximum nystagmus right lagged maximum linear acceleration right, and zero eye velocity lagged zero acceleration along the left–right axis (0 and 180) For 10 rpm maximum eye velocity occurred when the linear acceleration was in the same direction as the fast phase of the ongoing response e g *g*-left augmented nystagmus left and minimum eye velocity occurred when linear acceleration was opposite in direction to nystagmus fast phase e g., *g*-right suppressed nystagmus left

Key Press and Postural Sensations

As with nystagmus, the key press responses and postural sensations were quite different for 10 and 30 rpm For 10 rpm the postural sensations were usually approximately veridical as indicated by the subject s verbal description and his key press responses Subjects perceived continuous rotation about a horizontal axis and accurately estimated nose-up and nose-down positions There were two exceptions to the accurate perception of rotation and these were given by the two subjects who produced revers ing nystagmus during 10 rpm Both reported disorientation and were un able to signal positions by key pressing during rotation in the direction which produced reversing nystagmus The same subjects gave accurate signals of spatial positions and descriptions of body motion during rotation

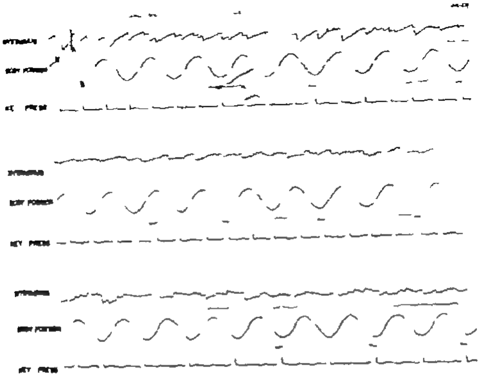
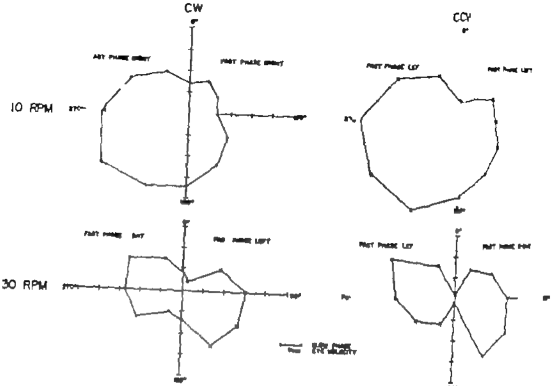


Fig. 6. Recordings showing coincidence of onset of reversing horizontal nystagmus and deterioration of position signals. Note that, as long as nystagmus is unidirectional, subject is able to estimate nose-up and nose-down positions.

directions which produced unidirectional nystagmus. After 20–40 sec at 30 rpm, all subjects, except one[1] exhibited responses similar to those of subjects with labyrinthine dysfunction (Guedry 1965) in that they were unable to estimate body positions accurately and their descriptions of body motions ranged from vertical-axis rotation to horizontal-axis rotation with the nose always pointing down or always pointing up. This disorientation usually began after about 30 sec of rotation at 30 rpm and was indicated by the inability of most subjects to signal accurately by the key press task during the remainder of the rotation interval. Those who continued to signal, though inaccurately, said that they were disoriented but attended to pressure cues for their estimates of nose-up and nose-down. During 30 rpm, the onset of disorientation was closely associated with beginning of the reversing nystagmus. As shown in Fig. 6 subjects signaled body position accurately while the nystagmus remained unidirectional; however, when the nystagmus started reversing (lower panel) the subject

[1] This single exception had unidirectional nystagmus and maintained essentially veridical spatial orientation throughout 30 rpm rotation.



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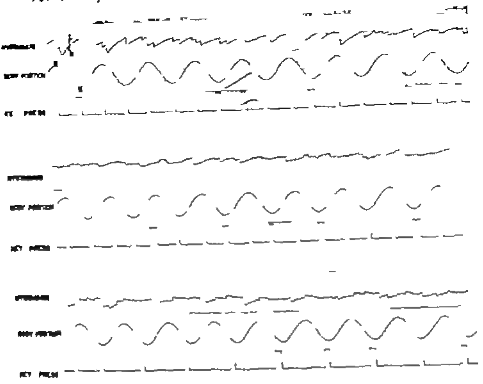

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no longer could estimate the nose-up position Many subjects either stopped key pressing altogether or gave signals which showed little relationship to true body position

Sickness

A high incidence of sickness was observed in this experiment Twelve of the twenty subjects were unable to complete the experimental sequence A relationship between mental task required of the subject and incidence of sickness was noted Of the twelve subjects who could not complete the sequence, all had been asked to attend to postural sensations with the purpose of giving accurate verbal and pictorial descriptions of the motion profile experienced during the runs Of the eight who completed, four were given the key press task and four were required to perform mental arithmetic during the rotation trials This relationship between sickness and mental task confirms similar earlier observations (Correia & Guedry 1964)

DISCUSSION

The time course of the nystagmus for the 10 rpm trials of the present experiment demonstrated the same general trend as that noted in previous experiments involving horizontal axis rotation (Benson & Bodin 1966 Guedry 1965) namely a sustained unidirectional horizontal nystagmus which persisted well beyond that observed for comparable vertical axis rotation Nystagmus at 30 rpm was continuous during the interval when the cupula would be theoretically deflected from the angular acceleration however a reversing nystagmus was observed after this period Generally subjects who produced a unidirectional response at 10 rpm produced a clear reversing nystagmus at 30 rpm for comparable time intervals of constant velocity rotation At 30 rpm when the reversing nystagmus commenced, the direction and magnitude of the nystagmus appeared to be related to the magnitude and direction of the gravitational linear acceleration vector along the subject s left–right (y) head axis This relationship between nystagmus and linear acceleration relative to the skull has previously been pointed out for several stimulus configurations including linear oscillation on a horizontal track (Niven Hixson & Correia 1965) Similarly at 10 rpm the orientation of the gravity vector relative to the horizontal head axes appeared to modulate the magnitude of the unidirectional nystagmus during the period of constant velocity as shown in Fig 5 Analysis of nystagmus during angular acceleration (footnote 1 page 300) and deceleration (Correia & Guedry 1964) demonstrates that reorientation relative to gravity influences nystagmus during these phases of horizontal axis rotation The peak nystagmic response was greater during acceleration and less during deceleration with the rotational axis horizontal as compared to rotation with the axis vertical These response differences are reasonable since during angular acceleration and reorientation relative

to gravity there is a coordinated input from both sets of stimuli during and after deceleration, sensory input is discordant. Upon being stopped (not reoriented relative to gravity) otoliths and pressure senses signal the stopped condition while the canals signal counterrotation in response to angular deceleration

To explain the continuous unidirectional nystagmus observed during horizontal-axis rotation at lower velocities, Benson & Bodin (1966) suggested that endolymph flow could develop due to differences in specific gravity of the perilymph and the endolymph filled membranous labyrinth It was further suggested that this mode of response would not persist at higher angular velocities where the dynamic properties of the membranous labyrinth, endolymph, and perilymph would limit continued responding by this mode. In the present experiment, a reversing nystagmus was observed as the rate of rotation was increased to a higher velocity This finding does not negate the Benson–Bodin hypothesis, but it does raise questions as to the latter being the only deviation from the commonly accepted mode of response during horizontal-axis rotation.

The finding of two types of nystagmus as a function of rate of rotation about a horizontal axis forces consideration of several modes of response for the canals and the otolith organs It is likely that both the semicircular canals and otolith organs act in concert during horizontal-axis rotation, but each may have a different response range and may shift response modes at different frequencies (rpm)

ACKNOWLEDGMENTS

The uthors wish to express appreciation for th fforts f L. J Roberts, AA, USN Mr A Thomas, M G T Turnipseed, and Mr J W Norman for their ssistance in thi experiment.

ZUSAMMENFASSUNG

Acht Männer unterzogen sich einem Experiment in dem si um ine erd horizontale Achse mit Geschwindigk iten von 10 und 30 Umdr /Min. rotiert wurden Nystagmus und subj ktive Schätzung der Körperlage im Raum waren beid mod fiziert be der höheren Tourenzahl. Versuchspersonen die im wesentlichen ichtige Schätzungen der Körperlage bei 10 Umdr /Min gaben, wurden disorientiert be 30 Umd /Min und machten Angaben die den von Versuchspersonen mit Funktionsstörungen des Labyrinths nah glichen. Versuchspersonen die inen d uernden gleichgericht ten h rizontalen Nystagmus bei konstanter Rot tion mit 10 Umdr Mi zeigten reagiert n mit umgek hrtem horizontalem N st gmus w hrend vergl ichbarer Zeitintervall der Rotation mit 30 Umdr./Min D Geschwindigk it des Nystagmu in gsamer Phase igte bei 10 und 30 Umdr Min. in zyklische Modulation, die von der Orientierung relati zur Schwerkraft abhing. Wi in *früheren Studien* igt sich Krankh it bei Rot tion um ein horizontale Achse und es wurde wiederum in Beziehung zwischen geistiger Beschäftigung und Krankheitsanfälligk it beobachtet.

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PHYSIOLOGICAL MECHANISMS OF PHONATION

TENSION OF THE VOCAL FOLD MUSCLE

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A method was devised to determine in situ, in the dog, the mechanism by which tension is developed in the thyroarytenoid muscle (vocal fold). The origin of the muscle was dissected from the thyroid cartilage and tied to a force transducer; the arytenoid cartilage was fixed. The recurrent laryngeal nerve was electrically stimulated with square wave pulses. Development of isometric tension was measured as a function of in situ resting length (L_o) and of the strength and frequency of the stimulus. In addition a passive tension length curve was constructed from L_o to 1.3 L_o. Tension increased sigmoidally with changes in initial muscle length, stimulus voltage and frequency, reaching a maximum at 1.2 L_o and 120 pulses/sec. Vocal fold tension, a factor in determining fundamental frequency of phonation, was found to be a complex function of the above variables. Clinical implications of findings were discussed.

INTRODUCTION

In the normal production of voice the generating source of the fundamental frequency of phonation is the larynx. The vocal folds of the larynx, or generator, modulate the intratracheal air flow to produce sounds of varying frequencies. The commonly accepted theory of action of the vocal folds in the production of the fundamental frequency of voice is generally referred to as the "myoelastic aerodynamic" theory of phonation. According to this theory the vocal folds are adducted and regulated in tension, mass and length by the intrinsic and extrinsic neuromuscular system of the larynx; they are further actively set into vibration and kept in motion by the intratracheal pressure and their own elasticity. Once the folds are adducted and set in mass, length, and tension, their state may be viewed as constituting a more or less static mechanism, while their active functioning is regulated by the intratracheal air pressure and musculature.

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A change in any variable as the length and tension of the vocal folds or subglottic area pressure, can produce a difference in the fundamental frequency (pitch)of phonation Studies have been made for example of the effects on vocal pitch of altering the variables of length and tension no work has been found however in which the neuromuscular mechanisms of vocal fold tension have been studied

REVIEW OF THE LITERATURE

Numerous investigations have been made on the mechanism of vocal pitch since Ferrein (1741) introduced the term *cordes vocales* in 1741 Ferrein was one of the earliest researchers to demonstrate that increasing the tension of the vocal folds and narrowing the distance between the cricoid and thyroid cartilages increased pitch Ferrein s observations have been confirmed by Curry (1940) and Sonninen (1954) with lateral laminograms Using human cadaveric tissue Van den Berg & Tan (1959) confirmed Mueller s (1843) experiments by demonstrating that vocal pitch could be changed by varying the tension of the vocal folds The vocal folds were stretched by weights, and measurements of longitudinal force recorded Later Longet (1841) confirmed the findings of the Rev Willis (1829) that contraction of the cricothyroid muscle draws the cricoid cartilage up to the thyroid cartilage thereby lengthening the vocal cords. Hollien (1960) found that when the vocal cords were in the primary position vocal fold length increased with a rising fundamental frequency of phonation

Employing the technique of electromyography Arnold (1961) corroborated Katsuki s (1950) and Faaborg Andersen s (1957) findings that electrical activity increased in the cricothyroid muscle with rising pitch In addition Faaborg Andersen found that with rising pitch, electrical activity increased in the cricothyroid muscle 0 9 second before an increased potential was seen in the vocal muscle Contraction of the cricothyroid muscle causes an increase in vocal fold tension and this has been confirmed in animal studies by Fessard & Vallancien (1957) and Isshiki (1959) This increase in vocal fold tension is in contrast and in addition to the tension resulting from contraction of only the thyroarytenoid muscle For as Arnold points out

> It follows that the cricothyroid s primary function is that of crude or *external vocal cord tension* Because this tension is achieved by increasing elongation of the cords with rising pitch it is an isotonic tension In contrast the fine or *internal cord tension* from subsequent contraction of the internal thyroarytenoid (or vocalis) muscle occurs with equal cord length for a given pitch level and represents an isometric tension consequently the cricothyroid and the vocalis are synergists with different modes and purposes of function

More recently Rubin (1963) stimulating the recurrent and superior laryngeal nerve of dogs, observed that contraction of the cricothyroid

muscle raised vocal pitch to a greater degree than does contraction of the thyroarytenoid muscle alone. In addition, Rubin corroborated Hast's (1961) and Dunker & Schlosshauer's (1958) findings that changes in vocal pitch were responsive to changes in the voltage but not the frequency of the electrical stimulus. Contrarily Isshiki (1959) observed a rise in vocal pitch with increasing frequency of neural stimulation.

A review of the literature cited above clearly shows that research on the function of the cricothyroid and thyroarytenoid muscles has received a considerable amount of attention. However a study has not been made of the mechanisms by which tension is produced in the contracting thyroarytenoid muscle.

The purpose of this investigation was to study the mechanism by which tension is developed in an isometrically contracting thyroarytenoid muscle, as a function of its initial length and of the strength and frequency of an electrical stimulus.

METHODS

Mongrel dogs were anesthetized with an intravenous injection of pentobarbital sodium (Nembutal, 30 mg/kg) With the animal in the supine position, a vertical midline incision was made from the level of the hyoid bone to the superior border of the manubrium of the sternum. The pretracheal muscles were separated medially and carried laterally to the trachea and the larynx tracheotomy was performed and an endotracheal cannula inserted to maintain a free air passage. The recurrent laryngeal nerve was freed from the surrounding connective tissue approximate 3 cm from the nerve's entrance into the larynx. A midline incision was made from the thyrohyoid membrane through the thyroid cartilage, along its prominence, and through the cricothyroid ligament to the superior border of the cricoid cartilage Then one of the alae of the thyroid cartilage was incised laterally (1 cm) at the level of the laryngeal sinus the incision was continued caudally parallel to the midline incision, to the inferior borders of the thyroid cartilage The incision was completed by cutting the cricothyroid ligament and anterior portion of the cricothyroid muscle Additionally the *in situ* resting length (L_o) of the thyroarytenoid muscle[1] was measured before the section of thyroid cartilage was dissected free.

[1] A study was made of the structure, anatomical relationships, and course of the muscle fibers of the dog's vocal fold. A number of dog larynges were serially sectioned, stained with H and E, and examined by light microscopy It was found that the thyroarytenoid muscle in the dog, as in the human, is composed of two distinct bundles of muscle: The thyroarytenoideus externus and thyroarytenoideus internus (vocalis) But as the two muscles cannot be separated surgically without damaging either muscle fibers or nerves the thyroarytenoid was treated physiologically *in toto*, as one muscle in this study The average length of this muscle for all animals was 16 mm.

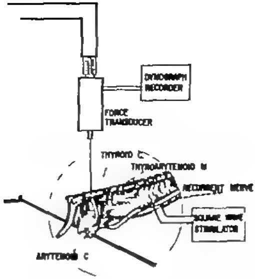

FIG 1 Diagram of method for measuring and recording total and passive tension of an *in situ* thyroarytenoid muscle

A length of surgical silk (3-0) then was sutured to the incised section of thyroid cartilage which is the point of origin of the thyroarytenoid muscle (true vocal fold) With the thyroid cartilage and thyroarytenoid muscle *in situ* the other end of the silk thread was tied to the input probe of a force transducer (Statham C1 16-350) (Fig 1) The point of insertion of the thyroarytenoid muscle, the arytenoid cartilage was fixed by piercing it with a large hypodermic needle (no 17 5 cm) clamped to a stand

The transducer was rigidly fixed to an adjustable rod that was scaled in millimeters the scaled rod was attached to a stand The total fixture could be adjusted so that the direction of sensitivity of the force transducer could be brought in line with the direction of the fibers of the muscle and the length of the muscle measured The output of the transducer was led to the input of a strain gauge coupler (Offner Type 9803) whose output was amplified and recorded by an ink writer (Offner Type RS Dynograph) The force transducer was calibrated in g wt (gram weight) with metric masses

The recurrent laryngeal nerve was electrically stimulated by square wave pulses from a physiological stimulator (Grass S-4) with coupled stimulus isolation unit (Grass SIU-4B) with bipolar platinum shielded electrodes The nerve was kept moist by a physiological irrigating solution (Baxter Tis-U-Sol) Animals were sacrificed at the end of the experiment

PROCEDURE

After developing and refining the above methods on an initial series of dogs, values of muscle tension measured in g wt., were collected on

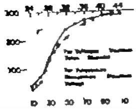

FIG. 2.

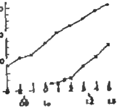

FIG. 3.

FIG. 2. Mean values of isometric tension developed by the thyroarytenoid muscle as function of the voltage and frequency of stimulation at 1.3 L_0. Ordinate is tension (g wt.); upper scale of the abscissa is voltage; lower scale of the abscissa is frequency in square wave pulses/sec.

FIG. 3. Total tension-length curve for an isometrically contracting thyroarytenoid muscle stimulated at 90 pulses/sec (upper curve) and passive isometric tension-length curve (lower curve) for the same muscle. Ordinate is tension (g wt.); upper scale of the abscissa refers to muscle length in mm; lower scale of the abscissa refers to the resting length (L_0). Muscle length 17 mm.

10 other dogs (10–14 kg). Animals were stimulated during the time interval between the inspiration–expiration periods of respiration. To avoid physiological summation, a 10 second interval between neural stimulation was maintained. The duration of each stimulus pulse was 0.25 msec, and trains of stimuli were limited to approximately 1 sec.

Recordings of muscle tension (g wt.) were made during stimulation with voltages from threshold to maximum, at frequencies from 10/sec to 120/sec, and at various muscle lengths from 0.8 to 1.3 L_0. In addition, passive tension was recorded at muscle lengths of L_0 to 1.3 L_0.

Four measures of muscle tension were obtained for each dog: (1) the passive tension at different lengths of muscle, (2) the isometric tension of the muscle as a function of the voltage of a train of stimuli, (3) the isometric tension of the muscle as a function of the frequency of a train of stimuli, and (4) the isometric tension of the muscle as a function of its length at maximal frequency of stimulation.

RESULTS

The maximum tension developed by the thyroarytenoid muscle in an isometric contraction at maximum voltage and supramaximal tetanic stimulation was at 1.3 L_0; muscle tension (g wt.) ranged from 215–355 g, with a mean of 292 g.

Both the strength and frequency of stimulation affected the tension developed in the muscle. The mean values for each variable at 1.3 L_0 are shown in Figure 2. Figure 3 illustrates the values developed for passive tension and total tension (active plus passive tension) as a function of muscle length, in one of the dogs. Although maximum total tension was

developed at 1.3 L_0, the maximum active tension (total minus passive tension) was at 1.1 L_0.

Most muscles reached maximum isometric tension with frequencies of stimulation of 90–100/sec. Only two animals showed a further increment of tension at 120/sec. Once the maximum frequency of stimulation was established for each animal at L_0, all other measurements were made at that particular frequency. The average voltage applied to the recurrent laryngeal nerve was found to be inversely related to the length of the muscle. The values from threshold to maximal stimulation were 0.32–2.1 V at L_0 and 0.24–0.44 at 1.3 L_0.

DISCUSSION OF EXPERIMENTAL FINDINGS

From the results of the present study it appears that the tension developed by the thyroarytenoid muscle (intrinsic muscle of vocal folds) was a function of the strength (voltage) and frequency of the stimulus and of the initial length of the muscle prior to stimulation.

These findings are in accord with the characteristics of striated muscle in general. Previous investigators have shown that for muscles in the extremities of man and animals: (1) isometric tension developed by a muscle was a function of its length before stimulation and that tension was greatest when the muscle was longer than its *in situ* length (Rosenblueth, Alanis & Rubio 1958); (2) tension developed in an isometrically or isotonically contracting muscle bore a linear relation to the integrated muscle action potentials, i.e. motor unit discharge frequency and number of motor units activated, until a maximum tension was reached (Adrain & Bronk 1929, Bigland & Lippold 1954 *a*, 1954 *b*, Eccles & Sherrington 1930, Lippold 1952) and (3) greater muscle tension was developed with a lower integrated voltage and count of motor unit potentials if the muscle was increased in length (Close, Nickel & Todd 1960). In the present work on the thyroarytenoid muscle, a lower frequency and strength of stimulus were needed to attain a particular level of tension if the muscle was lengthened (to a maximum of 1.3 L_0) before stimulation.

In applying the findings of this research to a general theory of phonation, several observations can be made. There appears to be a complex relationship between the strength and frequency of the stimulus to the recurrent nerve and of the muscle length before stimulation. In this study tension could be increased in the vocal fold muscle by increasing the stimulus voltage or by holding voltage constant and raising the frequency of stimulus or by lengthening the muscle (Fig. 2). Hast (1961) and Rubin (1963) found that in order to achieve sufficient air pressure for phonation, the vocal folds had to be closely approximated and tensed. This was accomplished by stretching the vocal folds (Hast 1961) or contracting the cricothyroid muscle (Rubin 1963) and then stimulating the recurrent nerve at a frequency of at least 50 pulses/sec. Increasing voltage of the

stimulus resulted in an increased subglottic air pressure with concomitant rise in the fundamental frequency of phonation The resistance offered to intratracheal air flow was a function of the tension developed by the vocal fold muscles.

In the present work as the muscle was lengthened a lower strength of stimulus (voltage) was required for increasing tension (muscle contrac tion) Thi could be part of the mechanism employed by man and the dog for phonation, as the isometrically contracting thyroarytenoid muscle is lengthened by the isotonically contracting cricothyroid muscle In addi tion passive thyroarytenoid tension at 130 per cent of resting length was equal to the total tension of the stimulated muscle at normal resting length (Fig 3) As stated above mechanical lengthening of the thyroarytenoid muscle simulated contraction of the cricothyroid muscle, and illustrated dramatically the effect of the cricothyroid on increasing vocal fold tension and therefore on vocal pitch

Also, it should be noted that at maximum length and frequency of stimulation tension increased in a sigmoidal manner (Fig. 2) with changes in the voltage f the stimulus, a relationship that also held for changes in stimulus frequency at constant voltage

The nature f the complex reciprocily shared by the two synergic muscles, cricothyroid and thyroarytenoid in the function of phonation cannot fully be explained by the findings of this study Knowledge obtained from research on the central mechanisms of laryngeal innervation is also required The experimental results of this study however may add to our technical understanding of the mechanism of vocal cord action The clinical implications of the findings in this paper are also of interest and should be considered.

CLINICAL IMPLICATIONS

One of the more important observations to emerge from the discussion of the experimental findings was that passive lengthening of the vocal fold (normally a *function of the external tensor* the cricothyroid muscle) produced in the thyroarytenoid muscle a degree of tension equal to that achieved in the normally lengthened vocal fold at maximal frequency of stimulation (Fig 3) *This illustrated the powerful* force exerted by the cricothyroid muscle in laryngeal functioning.

The above observation takes on particular significance in paralysis of the cricothyroid muscle The *typical* vocal syndrome is a weak or feeble voice lacking in projection while quickly fatiguing after brief efforts. Phonation-time is also shortened, as there is insufficient closure of the glottis, resulting in a loss of phonatory air With insufficient closure of the glottis there is also a lack f resonance or vocal intensity a result of decreased subglottic air pressure Other obvious symptoms, particularly noticeable in women, are a lowered vocal pitch and a narrowing of the vocal range (a monotonous singing voice)

developed at 1 3 L_0, the maximum active tension (total minus passive tension) was at 1 1 L_0

Most muscles reached maximum isometric tension with frequencies of stimulation of 90–100/sec. Only two animals showed a further increment of tension at 120/sec. Once the maximum frequency of stimulation was established for each animal at L_0, all other measurements were made at that particular frequency The average voltage applied to the recurrent laryngeal nerve was found to be inversely related to the length of the muscle The values from threshold to maximal stimulation were 0.32–2.1 V at L_0 and 0.24–0 44 at 1 3 L_0.

DISCUSSION OF EXPERIMENTAL FINDINGS

From the results of the present study it appears that the tension developed by the thyroarytenoid muscle (intrinsic muscle of vocal folds) was a function of the strength (voltage) and frequency of the stimulus and of the initial length of the muscle prior to stimulation

These findings are in accord with the characteristics of striated muscle in general Previous investigators have shown that for muscles in the extremities of man and animals (1) isometric tension developed by a muscle was a function of its length before stimulation and that tension was greatest when the muscle was longer than its *in situ* length (Rosenblueth Alanis & Rubio, 1958) (2) tension developed in an isometrically or isotonically contracting muscle bore a linear relation to the integrated muscle action potentials, i e., motor unit discharge frequency and number of motor units activated, until a maximum tension was reached (Adrain & Bronk 1929 Bigland & Lippold 1954 *a* 1954 *b* Eccles & Sherrington 1930 Lippold, 1952) and (3) greater muscle tension was developed with a lower integrated voltage and count of motor unit potentials if the muscle was increased in length (Close Nickel & Todd 1960) In the present work on the thyroarytenoid muscle a lower frequency and strength of stimulus were needed to attain a particular level of tension if the muscle was lengthened (to a maximum of 1 3 L_0) before stimulation

In applying the findings of this research to a general theory of phonation, several observations can be made There appears to be a complex relationship between the strength and frequency of the stimulus to the recurrent nerve and of the muscle length before stimulation In this study tension could be increased in the vocal fold muscle by increasing the stimulus voltage or by holding voltage constant and raising the frequency of stimulus or by lengthening the muscle (Fig 2) Hast (1961) and Rubin (1963) found that in order to achieve sufficient air pressure for phonation, the vocal folds had *to be closely approximated and tensed* This was accomplished by stretching the vocal folds (Hast 1961) or contracting the cricothyroid muscle (Rubin 1963) and then stimulating the recurrent nerve at a frequency of a least 50 pulses/sec Increasing voltage of the

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In the case of bilateral damage of the recurrent laryngeal nerve the function of the external tensor is of singular importance The classical description of this problem is well known Aside from a voice lacking in intensity or projection there are few vocal symptoms The most important diagnostic symptoms are short phonation time stridor and dyspnea these symptoms are often overlooked after thyroid surgery The powerful cricothyroid muscle, unopposed by the abductor muscle (posterior crico-arytenoid) is not only capable of lengthening and tensing the vocal folds for adequate vocal production but also adducts the folds to the paramedian position With an airway limited to 2 or 3 mm the problem of respiratory deficiency becomes paramount with the vocal deficiency of only secondary importance Woodman (1946) has devised an operative procedure that is frequently employed by the laryngologist for relief from this latter complication

The problem of bilateral abductor paralysis is not uncommon to the practice of otolaryngology and classical textbook descriptions of its symptoms abound The less classical but all too common immediate effect of complete bilateral recurrent nerve damage is a hoarse voice or loss of voice with little respiratory difficulty Perhaps after several months or years, a compensatory mechanism for adduction may result the voice improves and breathing becomes a problem Although a physiological explanation of the neuromuscular mechanism of this action cannot be completely described in this paper the experimental findings stated at the beginning of this section could give further insight into the above problems

CONCLUSIONS

An historical review of the literature on the action and function of the thyroarytenoid and cricothyroid muscles in the production of voice was made It was found that although the function of two of the parameters of vocal pitch length and tension of the vocal folds, has been described little attention has been given to the mechanism by which tension was developed in the vocal folds

A method was devised to measure isometric tension in the thyroarytenoid muscle as function of its length and of the strength and frequency of a neural stimulus

It was found that thyroarytenoid tension a factor in determining fundamental frequency of phonation increased sigmoidally as a function of initial vocal fold length and of the stimulus voltage and frequency

Maximum tension was reached at 130 per cent of the muscle's resting length with stimulation of the recurrent laryngeal nerve at 120 pulses/sec

Tension of the thyroarytenoid muscle was directly related to the length of the vocal fold and the frequency of the electrical stimulus and indirectly related to the strength of stimulus as the vocal muscle was lengthened

When the focal fold was passively lengthened to 130 per cent of its

in situ length, tension of the thyroarytenoid muscle was equal to that of the maximally stimulated muscle at normal length.

The action of the cricothyroid muscle (the external vocal fold tensor) is not only important in phonation but also is of singular clinical significance when the recurrent laryngeal nerve is damaged bilaterally.

ZUSAMMENFASSUNG

Eine Methode wurde entwickelt, an einem Hund *in situ* den Mechanismus zu bestimmen der für di Entwi klung von Zugspannung im *M. thyreo-arytenoideus* (Stimmfalte) verantw rtlich ist. Der Ursprung des Musk ls wurde vom Schild knorpel isoliert und an ein n Kraft Transducer angeschlossen der *C. arytenoidea* wurde starr gehalt n Der R kurrensnerv wurd durch Rechteckimpulse elektrisch gereizt. Das Anwachsen isom trischer Zugspa nung wurde al Fu ktion der *i situ* Ruhelänge (L_o) sowi der Intensität und Frequenz der Erregung ge messe Ausserdem wurde ei passive Spannungslängen Kurve für den Bereich von L_o bi 1.3 L_o ermittelt. Die Zugspannung wuchs bei Änderung der ursprünglichen Muskellänge der Erregerspannung und d r Erregerfrequenz S-förmig an und errei ht inen M ximalwert *bei 1.3 L_o und 120 Hertz. Die Spannung der* Stimmfalten in Faktor in der Bestimmung der Grundfrequen der Phonation, erwies sich ls in komplizierte Funktion der obengenannten Veränderlichen. Kli ische Anwendungen der Ergeb isse wurden diskutiert.

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ULTRASTRUCTURE OF LARYNGEAL PRECANCEROSES

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The authors have described the ultrastructure of the pachydermia, papilloma and the hyperplastic form of chronic laryngitis. These alterations result in the change of cell contact, pathological keratinization phenomena according to the behaviour of the nucleus and the cytoplasmic organelles can be regarded as precancerous changes. The continuance of the basal membrane breaks at certain points even in the precancerous alterations and the protuberances of the cytoplasm of the basal cells break through the epithelial-connective tissue border. Viruses could not be found in the papilloma.

INTRODUCTION

The ultrastructure of laryngeal precancerosis is little known as yet. Only the electron-microscopic structure of laryngeal papilloma has been studied in childhood and in adults (Friedmann, 1961; Meessen & Schulz, 1957; Svoboda, Kirchner & Pronel, 1963) in order to ascertain their viral origin. Pachydermia, hyperplastic form of chronic laryngitis and adult papilloma may be considered the precancerous alterations of the larynx. For details we refer to Leicher's monograph (1963).

In the present experiments we investigated the morphogenesis of laryngeal carcinoma, the manner in which the ultrastructure of the cells changes, their organelles, cell contact and epithelium—connective tissue border in the precancerous alterations, mentioned above, and in laryngeal carcinoma.

MATERIAL AND METHOD

In 27 patients, 29 excisions from the vocal chord and one from the epiglottis were performed. For light-microscopical diagnosis, part of the excision material was embedded in paraffin and the other part was examined under the electron microscope.

According to the clinical and histological diagnoses, our material is divided as follows: (*a*) 9 cases of normal mucous membrane, (*b*) 7 cases of pachydermia, (*c*) 6 cases of chronic laryngitis, (*d*) 3 cases of papilloma, (*e*) 1 case of initial carcinoma, (*f*) 3 cases of carcinoma.

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Fig. 1. The parabasal layer of the pachydermia. The intercellular space is dilated and contains intercellular debris (*ID*). The cytoplasm contains fine filaments (*F*). The basal membrane (*Bm*) is intact. Magnification 6600 ×.

In all the patients suffering from chronic laryngitis, focal hyperkeratosis was recognizable in the laryngoscopic picture Among the cases of pachydermia and chronic laryngitis (a total of 13 cases) pronounced atypia was recognizable in 5 cases at histological examination

For electron microscopic investigations the samples were fixed in OsO_4 according to Palade embedding was in araldite and staining with the combined method of uranylacetate and lead hydroxide (Karnovsky A) We established on the semithin sections stained with toluidin blue whether the material contained the alterations diagnosed The ultrathin sections were examined and photographed under an electron microscope JEM 6/c

RESULTS

The ultrastructure of the multilayered squamous epithelium of the vocal chord corresponds to the structure of the squamous epithelium of the mucous membrane (Fasske & Themann 1960 Haim 1964 Sognnaes & Albright 1956 Zelickson & Hartmann, 1962) Both in the intact and pathologically altered epithelium a basal intermediary and superficial layer could be distinguished apart from grave atypia or carcinoma being present The intermediate layer can be divided into a parabasal and a spongy layer

The basal membrane is well maintained in the *pachydermia* but it is conspicuous that even in the parabasal layer the spaces between the cells are dilated and intercellular debris appear (Fig 1) The filaments appear in fewer numbers and form a finer network They produce fascicles only in the parabasal and intermediate layers but the individual filaments remain well discernible in the fascicles Mitochondria are present in the parabasal and intermediate layers in conspicuously large numbers arranged around the nucleus and their matrices are markedly electrondense (Fig 2)

Mitochondrial dense bodies which were observed in the skin as a result of experimental carcinogenesis (Nakai, Shubik & Feldmann 1962 Selälä et al 1960 Sugár 1961) could not be demonstrated either in the pachydermia or the other precancerotic alterations The formation of thick structureless tonofibrils is particularly marked in the upper layer of the stratum spongiosum and here the filaments can only be slightly differentiated from one another or not at all Keratohyalin granules are present in very large numbers between the tonofibrils in the superficial layer (Fig 3) Almost all cell layers in the alteration contain cells rich in ribosomes, but particularly in the upper spongy layer epithelial cells with lighter cytoplasm and poor in ribosomes are observable The squamous epithelial cells contain relatively few endoplasmic reticulum, particularly the rough surfaced ergastoplasm has developed less Frequently the cisternae of the smooth surfaced endoplasmic reticulum are dilated, and in the vesicles so developed precipitation containing fine granules can be demonstrated (Fig 4) The Golgi zone is slightly developed though dense

Fig. 3 f. The superficial layer of the pachydermia, keratohyalin granules (Kh) are visible which are in close connection with the fibrils (F) partly sectioned transversely. G. Golgi zone. Magnification 7850 ×.

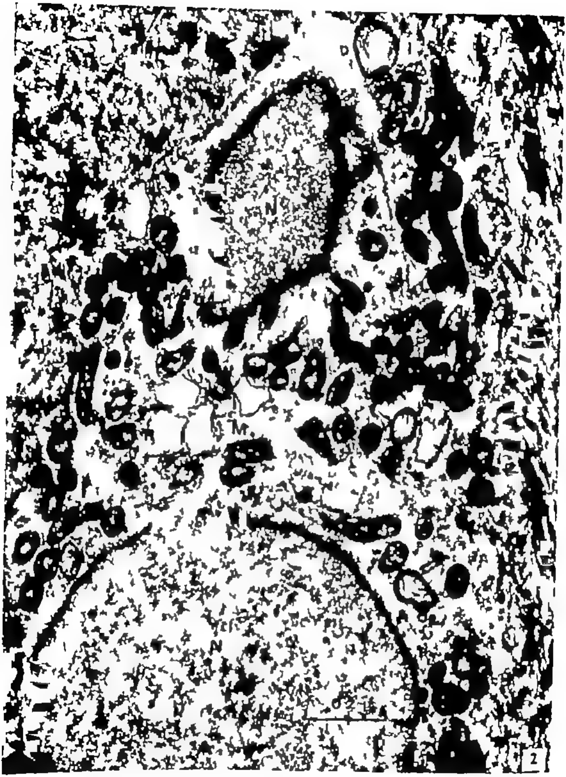
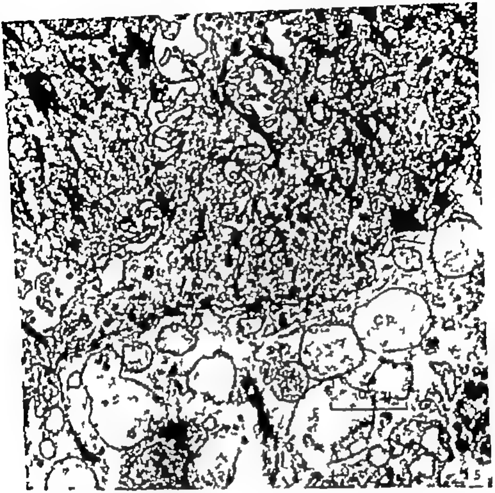


FIG. 2. Two nuclear parts (N) can be seen i th ll f th pa basal l y of the pachydermia. Numerous mitocho dri (M) are grouped rou d th nucleu th fila ments unite into fibrils (Fl). Th cistern f th smooth surfaced nd pla mic reticulum (ER) are dilated. Magnificati n 9700 2.6



| 5 The conti ace f the basal membrane (*Bm*) is broken t some point in the papilloma, nd here the cytoplasm formi g pseudopodi m-like protru ions (*Cp*) break through the basal membrane Most of the cytoplasmic protuberances f the pithelium re isible i the con ecti ti with the scepti f little ribosome subst nce, these cont i no othe struct ral lements. E en i the basal l yer the irregul formation of the fibril (*Fi*) nd thei ification from the filament ca be seen, a d the d lat tio of the i tercellula paces (*IS*) M gnification 2823 3.6

course The chromatin granules partly on the periphery of the nucleus are recogni ble and partly scattered in the karyopl sm. One or more nucleoli f rious izes and fairly irregular hapes can be found in each nucleus. Multinuclear cells r frequently recognized As an lectron microscopic gn of dy keratosi nd particularly in the uperficial layer smaller larger h rny ma ses develop which re partly found intracellularly and partly extracellularly The uppermost layer is frequently r miniscent of the tratum granulosum nd corneum of kin epidermis with keratohyalin gr nules nd numer us tran iti nal cells. A loosening of the cell contacts,

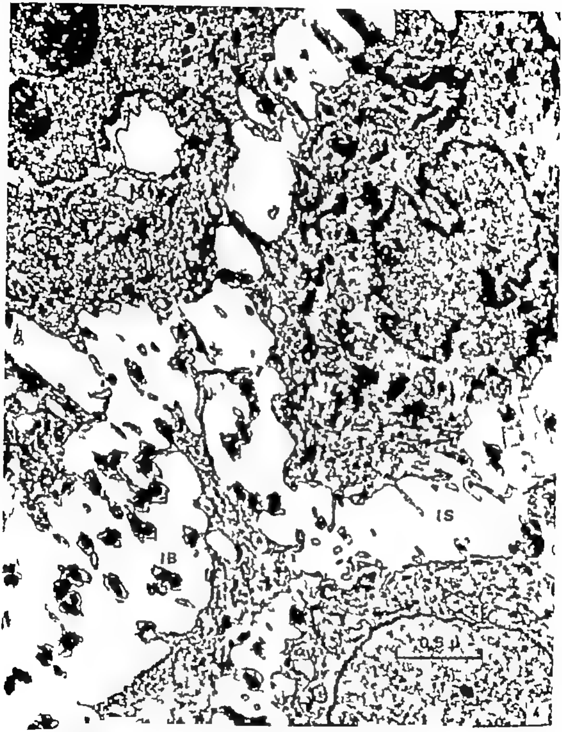


FIG. 4. The intercellular spaces (IS) are dilated [illegible] po[illegible] of the [illegible] epidermal; the intercellular bridges (IB) are broken [illegible] in the [illegible] t pl[illegible] m l[illegible] rg[illegible] les (V) have formed from the cistern[illegible] of the [illegible] d pla mi[illegible] ret[illegible] ul[illegible] m [illegible] gra[illegible] re[illegible] bl[illegible] the vesicles. Magnification 4000 × 2.6

bodies developed from numerous saccules are present mainly in the intermediate layer.

The cell nucleus, mainly in cases of atypia became irregular in shape and the double nuclear membrane produced deep furrows with a wavy

Fig. 3. The continuance f the basal membrane (Bm) is broken t some po t l the papilloma, nd here the cytopl m formi g pseudopodium-like protrusions (Cp) breaks through the basal membrane Most of the cytopl mic protuberances f the epithelium re isibl l the con ectiv tissue; with the xceptio f littl ribosome balance these cont l no other struct ral elements. E en i the basal layer the irregula forma-tion of the fibril (F) nd their ification from the fil ment can be seen, d the d lat tion of the intercell la spaces (IS) Magnification 3825 3.5

course The chromatin granule partly on the periphery of the nucleus are recognizable nd partly scattered in the karyoplasm. One or more nucleoli f v rion izes and fairly irregular shapes can be found in each nu leus Multinuclear cells are frequently recognized As an electron-micro-scopi ign f dy keratosi and particularly in the superficial layer smaller or larger horny ma ses develop which are partly found intracellularly and partly xtracellularly The uppermo t layer is frequently reminiscent of the trat m granulosum and corneum of skin epidermis with keratohyalin granules and numerous transitional cells A loosening of the cell contacts,

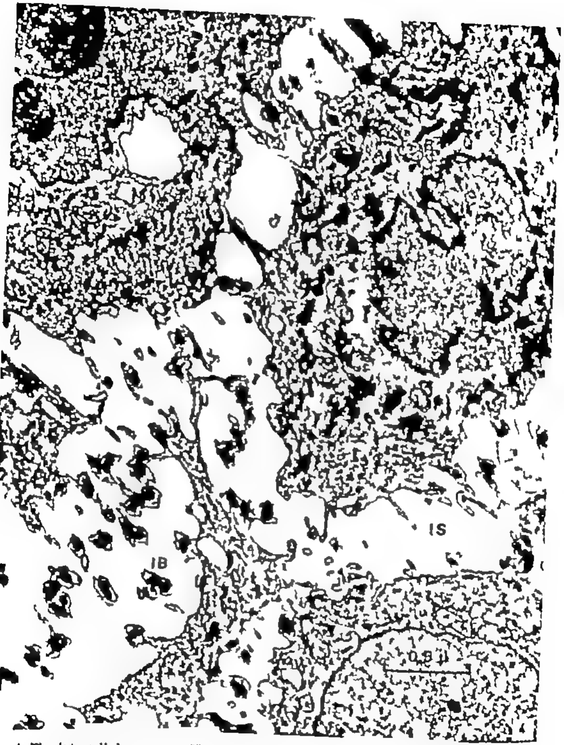


Fig 4 The int recllul pa (IS) re dil ted l tl pr ro l f tl pael derml th intercellular bridges (IB re brok n up in th t pl m l g esicl (l) ha e f rmed from the cistern f tl l pl mi reticul m f gra les re libl l the esicles Magnific tl 4000 2.6

bodies developed from numerous saccules are present mainly in the inter mediate layer

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FIG. 7. In the papilloma, the cytoplasm contains inclusion body (*I*) in which there are membrane contours and electrondense aggregates. The ribosomes ( ) are arranged like a rosette. *Mb* = multivesicular bodies. Magnification 6300 ×.

It is interesting that in these constricted cytoplasmic processes no filaments are visible. Dilatation of the intercellular spaces is conspicuous even in the basal layer. The alterations of the nuclear and cytoplasmic organelles are in many ways similar to those observable in the pachydermia. Frequently more nucleoli, 3 to 4, can be recognized in each nucleus; their shape and structure become irregular. It is noteworthy that the ribosomes form specific rosettes, and the tonofilaments unite into thick fibrils even in the basal layer. Apart from the ergastoplasm, multivesicular bodies can be seen, and large inclusion bodies could be recognized in the cytoplasm too (Fig. 7). These contain electrondense aggregates, in which membrane contours reminiscent of mitochondria and electrondense or less dense amorphic masses are mixed with electronlucent areas. A thick membrane surrounds the inclusions. Smaller dense bodies are observable in the cytoplasm. No virus particles could be demonstrated in the papilloma.

Carcinoma is the end stage of precancerosis; therefore in a few cases we examined the fine structure of cancer of the vocal chord.

All alterations characteristic for the ultrastructure of *keratinized squamous cellular cancer* were demonstrable in our material. In addition to irregularly branching and extremely changeable shapes and thicknesses of the tonofibrils (Fig. 8), large masses of Golgi vesicles and ribosomes arranged in rosettes were recognizable. Inclusion bodies in the papilloma are also frequently found. The thick and unified fascicles of the tonofibrils are conspicuous. There are tumour cells in which scarcely any fibril is present or within the cell filaments form a fine network. One of our cases was an extremely malignant and recurrent carcinoma. On the electron photomicrograph made from this tumour (Fig. 9) it could be recognized

Fig. 6. The cytoplasmic protuberance of the epithelium breaking through the basal membrane in the same papilloma as in Fig. 5 under greater magnification. × 10,800 35.

chiefly of those which are situated higher from the parabasal layer is characteristic of pachydermia and all precancerous cell alterations. As a result the intercellular spaces considerably dilate and smaller or larger cell debris of cytoplasmic origin, ribosomes and membranes are present. The structure of the desmosomes are usually undamaged, merely the cytoplasmic protuberances of the intercellular bridges have broken up and the development of cytoplasmic protuberances and microvilli are frequent in the intercellular spaces. No difference was noted in the ultrastructure of hyperkeratosis combined with chronic laryngitis and pachydermia.

The dermo-epidermal junction, i.e. the basal membranes of *adult laryngeal papilloma* is generally intact. However, certain places have been found where the basal membrane is lacking in circumscribed areas, and here the cytoplasm, producing a pseudopodium like protrusion, breaks through the basal membrane (Figs. 5 and 6). It is characteristic that these protruding parts over the basal membrane of the cytoplasm are poor in structure and scarcely contain ribosomes. On the electronmicrographs, the continuation of the cytoplasm protuberances in the connective tissue with the cytoplasm of the basal cells is seen to be mostly broken. However, certain protuberances have maintained their connection with the basal epithelium

FIG. 7 In the papilloma, th cyt plasm contains an inclusion body (*I*) in which there are membrane contours and lectronds se ggreg tes. The ribosomes ( ) re rranged like roseti *Mb* multi esicular bodies. Magnification 4200 3.5

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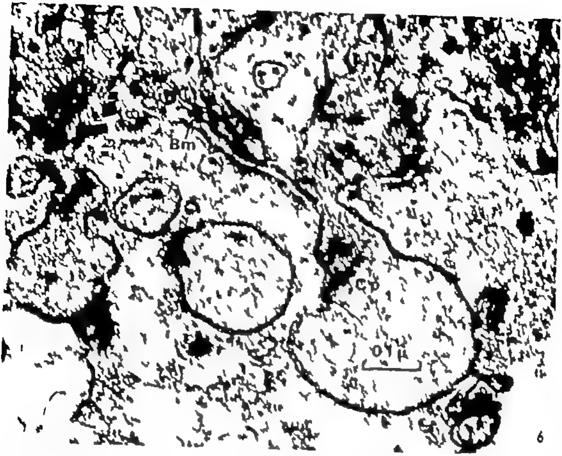

Fi 6 The cytopla mi protuberance of the pithelium breaki g through the basal membra e in th san papill ma a in Fig 5 and r great r magnific tion 10,800 ×.

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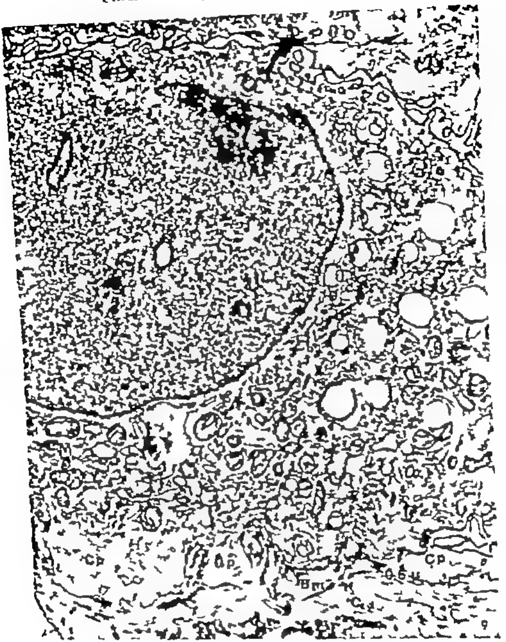

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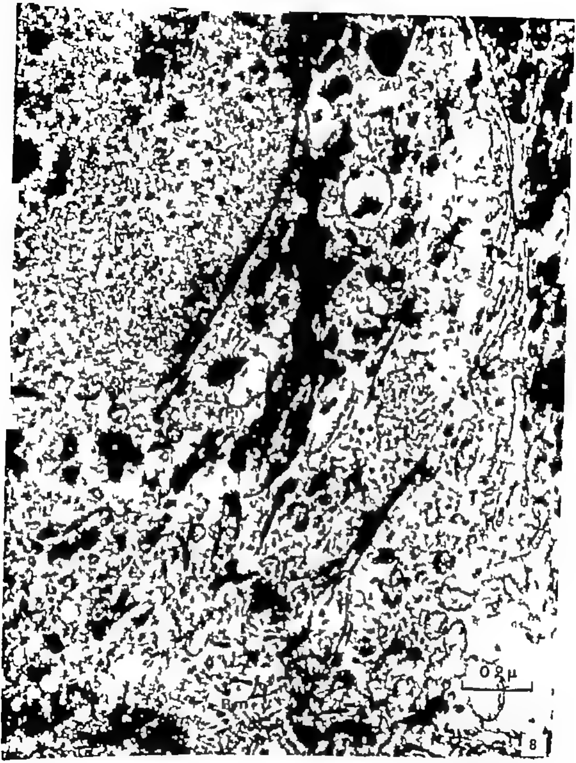

Fig. 8. Dense gra ules (D) are l ibl l th l l l yer f th k tl l ed pitheli l cancer in the ubstance between the c ll n leu hromatl The h pes f tl fibril (Fl) are irregul r and the l mentary fil m t l truct re l mo tly n recogni l l Bm basal membrane Magnificati n 8600 2.0

Fig. 9. T mo cell i the basal l er of th carcinomatou nest Only remna ts f the basal membrane (*Bm* re recognizabl The cytopl m ends wid processes (*Cp* to- ard the connect tissue these scarcely cont i y struct ral l me ts. The cyto- plasm cont ins ma y malal d maged m tochondri (*M*) which degenerat l k blisters. N nucleus *I* cytopla mic indentation; *L*, lipid granules; *D* desmosome *C*, collagen f bres M gn fication 1300 2 6

that the basal cell contained many degenerated mitochondria and filaments were scarcely present. The basal membrane is lacking in certain sections, and here the cell sends structureless pseudopodiums towards the connective tissue. The cytoplasm contains several Golgi zones and large amounts of multivesicular bodies. Many lipid granules can be found. Numerous cytoplasmic indentations are present in the nucleus.

DISCUSSION

According to clinicopathological investigations, laryngeal precanceroses can be classified in various stages in the processes leading to carcinoma. Kleinsasser (1959, 1961, 1962) distinguishes three stages: (I) epithelial hyperplasia of the simple cell without atypia which may be verrucoses and papillary; (II) epithelial hyperplasia with local circumscribed atypia of the cells; (III) precancerous epithelium in which extensive disturbances of differentiation reach a degree of carcinoma *in situ*.

The histological alterations observable with the electron microscope are: basal hyperactivity, superficial keratinization, parakeratosis and the formation of stratum granulosum in the otherwise non-keratinized squamous epithelium of several layers which is similar to that of its epidermis. Some cell nuclei may be enlarged in stage II and become hyperchromatic. Dyskeratosis may appear as a sign of pathologic keratinization. In the more advanced stage (III), all cellular changes characteristic of carcinoma can be found, but without infiltrative growth being demonstrable. We also classify laryngeal precanceroses according to similar ways and viewpoints (Polyánszky & Sugár 1959, Sugár 1961). The histological classification of Venkei & Sugár (1965) is similar to that of Kleinsasser (1962). Accordingly, precanceroses of skin cancers are grouped in three stages (A, B and C).

Thus, according to electron microscopic investigations, there are indications with which it is possible to draw conclusions concerning the precancerous nature of certain laryngeal alterations.

Electron microscopic investigations afford new information and help for the recognition of laryngeal precanceroses. The characteristics of atypia are essentially identical in pachydermia and in papilloma. In precancerous alterations, the cell contact and the ultrastructure of the cytoplasm and the cell nucleus change. Cell connection becomes loose and this is demonstrable both in the parabasal and in the basal layer.

The continuity of the basal membrane is lacking in sections of 0.05 to 0.1 mμ length, and here the cytoplasm forming pseudopodium-like protuberances reaches towards the connective tissue. In some cases very many cell protuberances are visible in the connective tissue which can be ascertained to originate from the epithelial cell, though the break through of the basal membrane, i.e. invasion over a wide front, is not yet noticeable. According to light microscopical investigations, Braun-Falco (1959) also

assumed that the continuity of the basal membrane ceases in laryngeal precarcinoma and not only in carcinoma. However the penetration of cytoplasmic protuberances has so far only been reported in skin cancers (Frei, 1962). The atypical arrangement of the fibrils indicates the pathological nature and presence of dyskeratosis, differentiation and keratinization. Cystic dilatation of the cisternae of the ergastoplasm and the vesicular alteration of the mitochondria are indicative of pathologic protein synthesis and cell degeneration. The free ribosomes are arranged in rosettes.

Th debris of cellular origin in the intercellular spaces and primarily the presence of ribosomes indicate cell destruction. The cell nucleus becomes irregular in shape even in precancerous alterations, its membrane runs a wavy course and its su face contains deep furrows. Cells with double nucl i are not rare. It seem that even in precancerous alterations inclusion bodies which contain structureles electrondense masses, membranes and cell debris can very frequently be found. These inclusion bodies can be demonstrated in carcinoma, too.

No viruses in laryngeal papilloma were found in accordance with other authors (Svoboda, Kirchner & Proncl 1963 Friedmann, 1961). The signs of keratinization in pachydermia are very similar to the keratinization of oral leukoplakia (Frithiof Lagerlöf & Wersall, 1963). In comparing the ultrastructure of laryngeal precanceroses with the alterati n developed during the morphogenesis of skin and uterus carcinoma (Albertini, Glatthaar & Vogel, 193 Setälä *et al* 1960 Sugár 1961) we believe that pachydermia, chronic laryngitis combined with hyperplastic hyperkeratosis and papilloma according to their fine structural alterations can be grouped among p ecancerosis.

ZUSAMMENFASSUNG

D Verfasser schildern di Ultrastruktur der hyperplastischen Form der h on schen Laryngiti sowie d ejenige der Pa hydermi und des Papilloms des Kehlkopfes. D ese Vera derungen können uf Grund der V änderung der Zell erbindungen der path logischen Ve hornungserschein gen sowie uf Grund des Verhalten der Organellen des Cyt plasmas l praecancerotisch Verä derun gen angesehen werd *Die Kontin ität der Basalmembran* wird n eine in n Punkten bere t im praeca cerotischen Stadium unterbrochen und di Auswüchse des Cytoplasma d Basalzellen durchbrechen d e Gre ze des Epithel-Bindegewebe Im Papillom gelang nicht, Viren na hzuw ise

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EEG IN MENIÈRE'S DISEASE

A Study of EEG and Caloric Directional Preponderance Before and After Ultrasonic Irradiation of the Labyrinth

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Abnormal EEGs were found in 12 out of 48 patients (25%) suffering from Menière's disease. No significant differences were noted between the preoperative EEG records and those performed 10 days after ultrasonic irradiation of the labyrinth. No significant correlation was noted between the EEG findings and the findings concerning caloric directional preponderance. Before treatment 28 patients out of 48 showed directional preponderance: in 17 directed from and in 11 toward the diseased labyrinth. After ultrasonic irradiation 33 patients showed preponderance: in 27 directed from and in 6 directed towards the diseased labyrinth.

INTRODUCTION

Menière's disease is characterized by a triad of symptoms—hearing loss (usually unilateral), repeated attacks of rotatory vertigo, and tinnitus. The examination reveals a sensory-neural loss of hearing, recruitment of loudness and in many patients a reduced caloric reaction often combined with a directional preponderance. The hearing loss is frequently worse before and during an attack of vertigo. The contribution of EEG to the diagnosis remains controversial.

The general opinion is that the lesion is localized to the inner ear: "endolymphatic hydrops" (Hallpike & Cairns, 1938; Lindsay, 1960; Schuknecht, Benitez & Beekhuis, 1962). The disease is bilateral in about 15% of the cases.

More than 200 patients with Menière's disease have now been treated with high frequency ultrasonic irradiation in the University Hospital in Uppsala. The rationale of this method is to selectively diminish the vestibular function of the inner ear and yet preserve hearing. There is no clinical evidence that neighbouring central nervous system structures are affected by the beam.

This investigation examines (1) the results of EEG from a group of advanced Menière's cases, (2) the possibilities of CNS damage due to

[*] Swedish Institute travelling fellow.

spread of irradiation during ultrasound treatment by comparing EEG findings before and after the procedure and (3) the correlation of EEG findings with caloric reactions (directional preponderance)

SUBJECTS AND METHODS

The *material consisted of 48 patients* (12 women and 34 men) with severe Menière's disease (mean age 46 years) with a mean duration of the disease of 8 years. All patients were incapacitated by frequent attacks of vertigo that were unmitigated by available medical treatment

The ultrasonic treatment is performed under local anaesthesia after mastoidectomy and exposure of the lateral labyrinthine wall Penetration of the ultrasound is facilitated by reducing the thickness of the bony capsule in a small area behind the lateral semicircular canal (Fig 1) against which the tip of the transducer is directed The ampullae and the vestibule lie beneath this thin layer of bone

During the irradiation the patient shows a strong nystagmus with the fast phase directed towards the irradiated side irritative nystagmus. After 3–20 minutes of irradiation the nystagmus usually reverses direction towards the contra lateral side "paralytic nystagmus This latter type of nystagmus usually remains for about a week and is thought to indicate elimination or reduction of the labyrinthine function on the operated side The patient complains of moderate vertigo and a sensation of off balance" during a few weeks following the operation

Details of the ultrasonic procedure and its results are given in previous reports (Sjoberg *et al* 1963 Sjoberg 1964 Stahle & Sahl 1964 Sjöberg & Stahle 1965)

EEGs were recorded from each patient a day or two before irradiation and about 10 days after Eight or 16-channel recordings were taken twenty one electrodes placed in the manner described by Penfield & Jasper (1954) Both bipolar (transverse and longitudinal) and "average reference leads were used in all cases The subjects were kept awake during the recording and care was taken to note early signs of drowsiness Hyperventilation and photostimulation were done routinely

Two electroencephalographers independently evaluated and classified the records without knowledge of identification by subject or time of recording Minor discrepancies in evaluations were easily resolved to arrive at a final classification upon which both raters agreed

Electronystagmography (ENG) according to the technique used in Uppsala (Aschan Bergstedt & Stahle 1956) was performed in connection with the caloric test before and after the irradiation The reactions were interpreted according to the rules given by Stahle (1958) and Stahle & Sahl (1964) The postoperative caloric testing 9–10 days after irradiation corresponded closely with the time of the second EEG recording

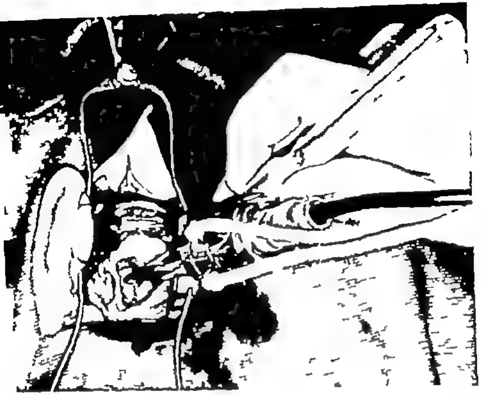

FIG. 1 The ltrasonic transducer is pplied t the lateral l byrinthi w ll through a post uricular pproach. The tip f the tra sducer is placed I prepared groov l the gle bet een the lateral nd the superior ertical canals. The beam i directed toward the mpullae nd the estibule

RESULTS

Th only EEG abnormality found among the patients was an episodic ppearance of slow waves in one or both temporal or fronto-temporal regions. The records were classified into four groups (1) normal (N)—mainly rhythm of 8–12 cycles per sec (2) "slight (S) episodic abnormality—recurring episodes of theta waves of low or moderate amplitude waves, clearly distinguishable from background activity (3) moderate (M) episodic abnormality—frequent episodes of theta o delta waves with an mplitude about twice that of the background rhythm (4) di tinct" (D) episodic abnormality—recurring episodes of delta waves or irregular com plexes with an amplitude more than twice that of the background activity

No abnormalities of epileptic type i.e pikes or sharp waves, were seen in any tracing

The preoperative EEG

As shown in Table 1 12 patients (25%) had n abnormal preoperative EEG

TABLE I. *Pre-operative EEG in 48 patients with Menière's disease*

		Abnormal EEG		
No. cases	Normal EEG	Slight	Moderate	Distinct
48	36	6	4	2

Correlation between preoperative EEG and side of diseased labyrinth

Among the 36 patients with an initially normal EEG, 15 were operated on the left side and 21 on the right.

Among the 12 patients with an initially abnormal EEG, 10 were operated on the left side and 2 on the right.

The temporal abnormality was strictly left-sided or showed left-sided predominance in 6 cases and in the remaining 6 cases the abnormality appeared symmetrically (side-shifting or bilateral synchronous episodes).

All 6 patients with a left-sided EEG abnormality were subsequently operated on the left side; 4 of those with a symmetrical EEG abnormality were operated on the left side, 2 were operated on the right.

Comparison between the pre- and postoperative EEG

Among the 12 patients with abnormal EEG records, 3 showed regress and 2 progress of the abnormality after the operation. Thus two patients changed from group S to N and one patient changed from group M to S. Those showing progress changed from group S and M to D (one case showed reversal from left to right-sided predominance).

Among the 36 patients with an initially normal EEG, 32 remained normal, whereas 4 showed a slight episodic abnormality after the operation (2 symmetrical, 1 left-sided and 1 with right-sided predominance).

Comparison between EEG and caloric directional preponderance (DP)

There is evidence that caloric or rotatory vestibular stimulation in humans—besides unspecific arousal reactions—can evoke specific changes of the EEG patterns in the temporal and posterior region (Zirmunskaja & Joselevič 1961, Makarjan & Koreskov 1961, Karbowski, Moor & Martin 1963, Barac 1966). It may be assumed that a disturbance of vestibular function—such as occurs during Menière attack, and also during and soon after ultrasonic treatment—is reflected in the EEG in a similar way.

In the present study EEG recordings were not taken during Menière attacks or the operation. However, many pre- and postoperative caloric tests revealed not only a reduced excitability of the labyrinth affected but also directional preponderance (DP), a sign indicative of central vestibular dysfunction (Fitzgerald & Hallpike 1942, Andersen, Jepsen & Kristiansen 1954, Kirstein & Preber 1954, Carmichael, Dix & Hallpike 1955) even though it often accompanies peripheral vestibular lesions (Cawthorne, Fitzgerald & Hallpike 1942, Stahle 1958, Koch *et al.* 1959,

TABLE 2

	Directional preponderance		
EEG	Present before and/or after operation	Absent before and after operation	
Abnormal before and/or after operation	15	1	16
Normal before and after operation	26	6	32
Total	41	7	48

Coats, 1965). The following results were obtained when the findings concerning DP were compared to the EEG findings before and after the operation.

The caloric reactions of 48 patients *before ultrasonic treatment* showed (1) no directional preponderance in 20 cases, (2) directional preponderance in 28 cases, in 17 directed from and in 11 towards the diseased labyrinth.

Of the 12 patients who showed an abnormal EEG before treatment 9 also showed nystagmic directional preponderance. *Of* the 36 patients who initially showed a normal EEG 19 showed such DP. No preoperative correlation was noted between the direction of the nystagmic preponderance and the side of the EEG abnormality.

A comparison of the caloric responses *10 days after operation* with the preoperative record showed DP changes in 28 cases. These changes were as follows: (1) from normal reaction to DP in 13 cases, in 10 cases preponderance from and in 3 towards the diseased ear; (2) *reversal of the* DP in 7 cases, in 6 a DP from and in 1 a DP towards the *affected ear;* and (3) normalization in 8 cases. Thus the operation produced a DP *from the* operated side in 16 cases and towards the operated side in 4 cases.

The postoperative EEG in 9 patients had changed qualitatively to some degree. However *the direction of the* postoperative nystagmographic *changes were not related to the EEG changes.*

Table 2 shows the results obtained when *the group* of patients with abnormal EEG findings are compared with *the* group with normal EEG both before and after the operation, with regard to the presence or absence of directional *preponderance before* and/or after the operation. It may be of interest to note that *the majority of the* patients which never showed DP also had a normal EEG (in 6 out of *7 cases*).

COMMENTS

1. Many normal adult individuals exhibit recurring episodes of theta waves over the temporal regions and such episodes usually show a left sided predominance. Our percentage of "abnormal" preoperative EEGs

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COMMENTS

1 Many "normal" adult individuals exhibit recurring episodes of theta waves over the temporal regions and such episodes usually show a left sided predominance Our percentage of "abnormal preoperative EEGs

(25%) does not exceed the incidence of similar abnormal findings in control groups of "normal" adults (Mundy-Castle 1951, Frey 1961, Kool *et al.* 1964). It is of interest to note that Petersén, Steinwall & Welander (1959) found EEG abnormalities in 4 out of 15 Menière's cases, whereas such abnormalities were more common in cases of benign positional nystagmus (10 out of 25). The common traumatic etiology of the latter syndrome, however, may contribute to this high rate of abnormalities (Stahle & Terins 1965). Niedermeyer & Hinchcliffe (1965) also found a relatively small number of abnormal records in patients with Menière's disease (5 out of 27) as compared to patients with vertigo due to other causes.

2. Abnormal EEGs were found more frequently in patients with a left sided disease; in contrast most patients with symptoms from the right labyrinth exhibited a normal EEG. Since our subject sample is relatively small we cannot establish a significant positive correlation but the observation deserves to be noted.

3. No significant discrepancy was noted in the majority of our patients (39) between the pre- and postoperative EEG record. The discrepancies found in the remaining 9 cases were so small and of such inconsistent character that they may be regarded as random variations. *Consequently our results give no evidence that the irradiation causes brain damage which may be recognized by means of ordinary EEG examination.*

4. The prognostic value of the EEG in these particular cases was evaluated by comparing the degree of abnormality of the initial EEG with the curative effect of the operation as regards the attacks of vertigo. All but 5 patients improved after the operation. In four of these cases the initial EEG was normal. Thus it appears that a moderate or distinct episodic temporal abnormality in the preoperative EEG does not indicate a less favourable effect of irradiation.

5. Proceeding from the assumption that directional preponderance is an expression of a central vestibular disturbance which may result from a brain lesion or a lesion in the labyrinth, we have compared the EEGs and the caloric reactions. It was not possible to establish any definite relation between the EEG findings and the findings concerning directional preponderance, either before or after the ultrasonic treatment. Of the 36 patients with normal EEG, more than half showed a directional preponderance.

Lack of directional preponderance both before and after operation was found more often in patients with normal than in patients with abnormal EEGs.

6. A preoperative directional preponderance – in most patients combined with a reduced caloric excitability – has been recorded in 58% of the patients. This figure is somewhat higher than the per cent reported previously. The reason for this difference probably is that electronystagmography has improved our ability to detect even a moderate DP.

After unilateral ultrasonic irradiation of the labyrinth the frequency of directional preponderance was raised to 69% the dominant direction was from the treated ear (in 27 out of 33 patients) This result is consistent with our aim to reduce the vestibular function of the diseased inner ear by irradiation. In 6 patients the postoperative preponderance was directed towards the treated ear This result however does not exclude a reduced peripheral function. Such a homolateral preponderance might be analogous to a phenomenon called "recovery nystagmus" (Stenger 1959 Lange, 1965) which is directed towards the diseased ear and more rarely noted in partial labyrinthine lesions.

ZUSAMMENFASSUNG

Abnorme EEGs wurden bei 12 von 48 P tienten (25%) mit Menières Krank he t beobachtet. 10 Tage n ch abgeschlossener Ultraschallbehandlung a fgen m-mene EEGs zeigten k in eindeutige Abweichungen von praoperativen EEG-s. Eindeutige Übereinstimmung zwischen EEG und kalorischer Nystagmusbereit schaft konnt nicht festgestellt werden Vor der Ultraschallbehandlung zeigten 23 on 48 Patienten Nystagmusbereitschaft, in 11 Fallen zum krankhaften Lab y rinth hin und in 17 Fallen in entgegengesetzter Richtung. Nach Ultraschallbe-handlung zeigten 33 Pat enten Nystagmusbereitschaft, in 6 Fallen zum krank haften Labyrinth hin u d in 27 Fällen in entgegengesetzter Richtung.

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INTERACTING VESTIBULAR STIMULI AND NYSTAGMIC HABITUATION

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Fifteen normal male subjects were repeatedly exposed t interacting angular acceleration (a posi ve accelerati n immediately f llowed by a egative acceleration of equal inten ity and duration) Pre- and post-test trials, consisting of st ndard ingle angula ac lerations, permitted evaluation of the neces ty fo habituation of rest intervals between su cessively presented stim li. Since significa t response decrements were evident in both the post-test responses and esponses t the interacting stimuli, it wa concluded that nystagmi habituati may occur without nystagmus running to normal completion

Several experiments related to the habituation of vestibular responses to angular acceleration have indicated that if nystagmic responses are not permitted to run to normal completion nystagmic response decrements to repeated stimulation do not occur For example, Mowrer (1934) with pigeons, and Holsopple (1924) with man, varied the temporal intervals between successive accelerati ns and found that alternate periods of ac eleration and constant elocity were equired for a response decrement to take place If the "rest intervals" i.e the periods of constant elocity between successive accel rations, were too short then no habituation re sulted H lsopple interpreted these results as signifying that nystagmus decreases by virtue of having frequently run to normal completion and is not reduced *merely because of the frequent occurrence of it stimulus*" (1924 p 103) Indirect support for this interpretation is p ovided by a number of studies. Fearing & Mowrer (1934) found that while the nystagmic responses of unanesthetized pigeons habituat markedly with re peated testing, anesthetized birds show no response diminution Both groups were exposed to identical ccelerative stimuli but the anesthetized group yi lded n nystagmic responses during the habituating series while the unanesthetized bird demonstrated a normal response. This clearly implicates the occurrence of the response rather than simply frequent exposure t the stimulus as a controlling factor in nystagmic habituation. Other supporting evidence of a general nature stems from studies finding at least some tran fer of habituation between different modes of stimula tion f the semicircul r canals (Collins, 1964 *b* Dunlap, 1925) That is,

despite different stimulating techniques the nystagmus generated is quite similar and again nystagmic habituation appears to be response related and independent of the stimulus

However a number of experiments examining the same question of transfer of habituation have found little or no transfer of habituation between caloric and rotary stimulation despite the general similarities of the nystagmic responses generated (Collins, 1964 *a* Hood & Pfaltz, 1954 Maxwell Burke & Reston 1922) These findings along with the specificity of habituation with regard to direction (Collins, 1964 *a* Crampton 1962 *a* Henriksson 1961) and plane of rotation (Crampton & Brown 1964) clearly implicate stimulus properties as important aspects of habituation Furthermore even when nystagmus is inhibited in both its intensity and duration by requiring the subject to fixate a visual stimulus during the habituating series highly significant decrements still occur (e g., Brown & Crampton 1966 Crampton 1962 *b* Guedry 1965) These latter studies not only cast considerable doubt on the necessity of nystagmus running to completion for habituation to occur but also raise the issue of whether exposure to the stimulus independent of the occurrence of nystagmus may not be sufficient for habituation Since visual input in many cases completely inhibits vestibular nystagmus and since stimulus properties appear to play an important role in the transfer of nystagmic habituation this question is of particular significance

The present study approached the question of the necessity for habituation of 'rest intervals between successively presented stimuli However rather than varying the length of the period of constant velocity or inhibiting nystagmus by fixation of a visual stimulus the subject was exposed to a series of interacting vestibular stimuli i e., an initial positive angular acceleration followed immediately by a negative acceleration Although Graybiel & Clark (1952) examined oculogyral responses and Jongkees & Klijn (1956) studied rotary sensations resulting from these successively presented stimuli of opposite sign the effect of repeated exposure to these accelerations has not been evaluated Guedry (1954 1957 *a* 1957 *b*) identified these triangular waveform accelerations as interacting vestibular stimuli due to the reciprocal effects of each acceleration upon the other Although the nystagmus initiated by the first acceleration extends into the period of the second acceleration there is a brusque curtailment of the initial primary nystagmus as the cupula is rapidly returned from its extended position by the second acceleration Further the total nystagmic output to the second acceleration is extensively inhibited as compared to the generated by a single non interacting stimulus

It was hypothesized that if a rest interval between successive accelerations were critical no habituation would be found in nystagmic responses to the repeated interactive stimulation In addition to examining successive responses to the interactive stimuli pre and post habituation test trials

permitted an evaluation of the influence of the triangular waveform habituating series on the normal nystagmus resulting from single non interacting accelerations.

METHOD

Stimulator

The angular accelerator described in detail by Brown & Crampton (1964) consists of a hydraulically driven rotating beam that supports the subject's chair. The chair was placed so that the subject's head was over the rotatory axis and an adjustable bite board restrained the subject's head in a fixed position. A ventilating fan and small "dither" motor provided low level masking vibration and noise to prevent detection of extraneous signals. A lightproof capsule entirely enclosed the subject, permitted control of visual input, and eliminated velocity cues associated with air movement. Electronic voice communication between the subject and the experimenter was provided.

Recording

Electrodes were taped near the outer canthi of the eyes, and an indifferent electrode was placed in the center of the forehead. The signals for horizontal eye movements were led through slip rings to an ink writing recorder at the control console. Eye movement potentials were amplified with a 1.4-sec RC time constant and displayed with a 25 mm/sec paper speed. Both the periods of acceleration and signals the subject initiated by pressing a key were recorded. At the outset and at the end of each experimental session a calibration to convert from mm to degrees of slow phase eye movement was obtained.

Procedure

All testing was conducted in total darkness, and each subject was instructed to keep his eyes open and generally centered. The bite board maintained the subject's head in a fixed position. Fifteen male subjects free from labyrinthine disorders and ranging in age from 18–24 years received the series of angular accelerations shown in Table 1 in a single session of less than one hour's duration. The subjects had no previous laboratory acceleration experience. All accelerations were symmetrical around zero velocity and the pre- and post-test trials (trials 1, 2, 9 and 10) involved a velocity change of 40 rpm in 11 sec (from [illegible] rpm in one direction through zero velocity to 20 rpm in the opposite direction). For trials 3–8, the habituating series, the total velocity change was 80 rpm but in [illegible] sec. Here a positive acceleration brought the subject from 20 rpm in a CCW direction to 20 rpm in a CW direction, and was followed immediately by a negative acceleration which returned the subject to 20 rpm in a CCW direction. The subject had a signal key in each hand. He was

despite different stimulating techniques, the nystagmus generated is quite similar and again nystagmic habituation appears to be response related and independent of the stimulus

However a number of experiments examining the same question of transfer of habituation have found little or no transfer of habituation between caloric and rotary stimulation despite the general similarities of the nystagmic responses generated (Collins, 1964 *a* Hood & Pfaltz, 1954 *Maxwell Burke & Reston 1922)* These findings, along with the specificity of habituation with regard to direction (Collins, 1964 *a* Crampton 1962 *a* *Henriksson 1961)* and plane of rotation (*Crampton & Brown, 1964)* clearly implicate stimulus properties as important aspects of habituation Furthermore, even when *nystagmus is inhibited in both its intensity* and duration by requiring the subject to fixate a visual stimulus during the habituating series, highly significant decrements still occur (e.g Brown & Crampton 1966 Crampton 1962 *b* Guedry 1965) These latter studies not only cast considerable doubt on the necessity of nystagmus running to completion for habituation to occur but also raise the issue of whether exposure to the stimulus independent of the occurrence of nystagmus may not be sufficient for habituation Since visual input in many cases completely inhibits vestibular nystagmus, and since stimulus properties appear to play an important role in the transfer of nystagmic habituation this question is of particular significance

The present study approached the question of the necessity for habituation of rest intervals between successively presented stimuli However rather than varying the length of the period of constant velocity or inhibiting nystagmus by fixation of a visual stimulus, the subject was exposed to a series of interacting vestibular stimuli i.e., an initial positive angular acceleration followed immediately by a negative acceleration Although Graybiel & Clark (1952) examined oculogyral responses and Jongkees & Klijn (1956) studied rotary sensations resulting from these successively presented stimuli of opposite sign the effect of repeated exposure to these accelerations has not been evaluated Guedry (1954 1957 *a* 1957 *b*) identified these triangular waveform accelerations as interacting vestibular stimuli due to the reciprocal effects of each acceleration upon the other Although the nystagmus initiated by the first acceleration extends into the period of the second *acceleration there is a brusque curtail*ment of the initial primary nystagmus as the cupula is rapidly returned from its extended *position by the second acceleration* Further the total nystagmic output to the second acceleration is extensively inhibited as compared to the generated by a single non interacting stimulus

It was hypothesized that if a rest interval between successive accelerations were critical no habituation would be found in nystagmic responses to the repeated interactive stimulation In addition to examining successive responses to the interactive stimuli pre and post habituation test trials

permitted an evaluation of the influence of the triangular waveform habituating series on the normal nystagmus resulting from single non interacting accelerations

METHOD

Stimulator

The angular accelerator described in detail by Brown & Crampton (1964) consists of a hydraulically driven rotating beam that supports the subject s chair The chair was placed so that the subject s head was over the rotatory axis and an adjustable bite board restrained the subject s head in a fixed position. A ventilating fan and small dither" motor provided low level masking vibration and noise to prevent detection of extraneous signals. A lightproof capsule entirely enclosed the subject, permitted control of visual input, and eliminated velocity cues associated with air move ment. Electronic voice communication between the subject and the experi menter was provided.

Recording

Electrodes were taped near the outer canthi of the eyes, and an indifferent electrode was placed in the center of the forehead. The signals f r horizontal eye movements were led through slip rings to an ink writ ing recorder at the control console. Eye movement potentials were amplified with a 1 4-sec RC time constant and displayed with a 25 mm/sec paper speed. Both th periods of acceleration and signals the subject initiated by pressing a key were recorded. At the outset and at the end of each experimental session, a calibration to convert from mm to degrees of slow phase eye movement was obtained.

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The present study approached the question of the necessity for habituation of "rest intervals" between successively presented stimuli. However, rather than varying the length of the period of constant velocity or inhibiting nystagmus by fixation of a visual stimulus, the subject was exposed to a series of interacting vestibular stimuli, i.e. an initial positive angular acceleration followed immediately by a negative acceleration. Although Graybiel & Clark (1952) examined oculogyral responses and Jongkees & Klijn (1956) studied rotary sensations resulting from these successively presented stimuli of opposite sign, the effect of repeated exposure to these accelerations has not been evaluated. Guedry (1951, 1965 *a*, 1967 *b*) identified these triangular waveform accelerations as interacting vestibular stimuli due to the reciprocal effects of each acceleration upon the other. Although the nystagmus initiated by the first acceleration extends into the period of the second acceleration, there is a brusque curtailment of the initial primary nystagmus as the cupula is rapidly returned from its extended position by the second acceleration. Further, the total nystagmic output to the second acceleration is extensively inhibited as compared to the generated by a single non-interacting stimulus.

It was hypothesized that if a rest interval between successive accelerations were critical, no habituation would be found in nystagmic responses to the repeated interactive stimulation. In addition to examining successive responses to the interactive stimuli, pre- and post-habituation test trials

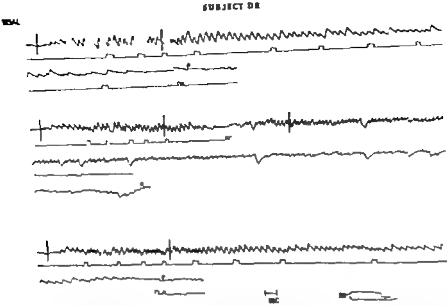


FIG. 1 Three records for a single subject are illustrated. Trial 1 and 9 are the pre- and post-test trial (positive angular acceleration) while trial 3 is the first of the interacting stimuli. The vertical bars define the periods of acceleration and the arrows show the transition points for the cycl gram. The key press responses are shown below the cycl gram record and the 20° calibration and time scale are also shown.

TABLE 2. *Summary of analyses of variance*

Source	*df*	SS	MS	*F*
A. Trials 1 and 9 (pos. accels.)				
Between Ss	14	.2063		
Within Ss	15	0760		
Trials	1	.0325	.0325	30.8
Residual	14	0244	.0017	
B. Trials 2 and 10 (neg. accels.)				
Between Ss	14	.2031		
Within Ss	15	0999		
Trials	1	0158	.0158	11.7
Residual	14	.0341	0030	
C. Trials 3–8 (interacting accels.)				
Between Ss	14	.9007		
Within Ss	73	.3161		
Trials	5	.06 0	.0131	3.4
Residual	14	.2791	.0040	

Sig. beyond .01 level

TABLE 1 *Summary of experimental design and stimulus characteristics*

Trial	Stimulus 22 /sec²	Duration sec	Velocity change rpm
1	Positive angular acceleration	11	40
2	Negative angular acceleration	11	40
3–8	Triangular acceleration	22	80
9	Positive angular acceleration	11	40
10	Negative angular acceleration	11	40

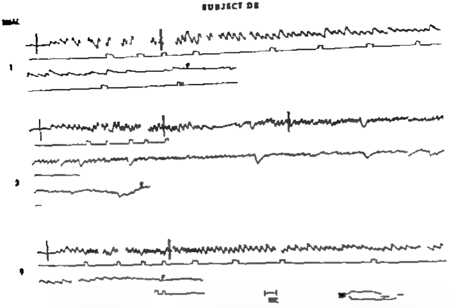
instructed to signal 90 of subjective arc by depressing the key appropriate to his direction of turning He also was instructed to signal a stop or change of direction with two key presses in rapid succession and then to continue the subjective estimation of velocity using the appropriate key The importance of this task was emphasized to the subject throughout the experiment in order to maintain a high level of alertness A minimum of five min of constant velocity was programmed between trials to control extraneous undesirable interactive effects

RESULTS

The vertical magnitude of the slow phase sweep of each primary nystagmic beat was measured in mm for each 1 sec segment of the record converted to degrees of slow phase eye movement by means of the calibration obtained at the end of each session and then summed across seconds for each trial A sample recording showing the nystagmic responses to the pre- and post test positive accelerations as well as responses to a triangular stimulus, are presented in Fig 1 Particularly to be noted is the sharp curtailment of the nystagmic and subjective responses to the initial acceleration as the second acceleration is imposed

Since previous work has indicated that geometric means are a more appropriate measure of central tendency for nystagmic data than arithmetic means (e g Crampton & Brown 1964 Brown & Crampton 1964) logarithmic transformations of the data were made All analyses were conducted on the transformed data and the figures are plotted as geometric means

To determine the influence of the interpolated interacting stimuli on the simple accelerations, responses to the pre and post test trials were evaluated by analysis of variance Separate analyses were performed on the pre- and post test positive acceleration trials (1 and 9) and on the pre and post test negative acceleration trials (2 and 10) These analyses are summarized in A and B of Table 2 and the data are plotted as part of Fig 2 Highly significant decrements in nystagmic output are evident from



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A. Trials 1 and 9 (pos. accels.)				
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Within Ss	15	.0[illegible]69		
Trials	1	.0523	0525	30 8
Residual	14	.0244	.0017	
B. Trials 2 and 10 (neg. accels.)				
Bet[illegible]een Ss	14	.2031		
Within Ss	15	.0690		
Trials	1	.0158	.0153	11 7
Residual	14	.0541	.0039	
C. Trials 3-8 (interacting accels.)				
Bet[illegible]een Ss	14	.9907		
Within Ss	75	.3461		
Trials	5	.06[illegible]0	.0134	3.4
Residual	14	.2[illegible]91	.0040	

Sig. beyond .01 lev[illegible]l.

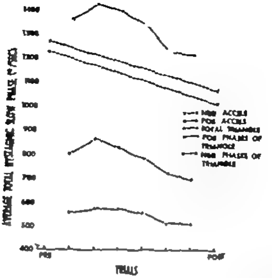

FIG. 2. Nystagmus slow phase averaged across responses from the 15 subjects, is plotted gainst trials Th dashed lines indicate the pre- and post trial while the solid lines indicate the interacting stimuli All data re plotted as geometric means.

the pre-test to the post test for both positive and negative accelerations. This decrement of nearly 20% is of the same order of magnitude as the decline found in an earlier study (Brown & Crampton 1966) where the subject was repeatedly exposed in the dark to an equivalent number of accelerations of similar intensity However in this earlier study the ha bituating series consisted of single non interacting accelerations The equivalence of these decrements seems to indicate that nystagmic habitua tion is not adversely influenced by the failure of the nystagmic reaction to run its normal course.

An important consideration related to the above discussion is the extent to which nystagmus slow phase decreases during the habituating series of triangular accelerations Do responses to both aspects of the interactive stimulus show systematic declines over the series of six trials? In Fig 2 the total slow phase output for primary nystagmus is plotted separately for each acceleration of the triangular stimulus, as well as for the total combined primary output The positive acceleration data includes nys tagmus summed over only the 11 sec of the initial positive acceleration while data for the negative acceleration was arrived at by summing over the output during both the negative acceleration and the ensuing constant velocity An analysis of variance of the combined output is summarized in C of Table 2 Nystagmic responses to both accelerations clearly habituate and the decrement for the combined output is statistically significant This is also evident in Fig 3 where these data are plotted second by second for the first and last interactive stimuli in the habituating series

Another interesting aspect of the triangular stimulus is the precise na ture of the nystagmic transition which shortly follows the onset of the

FIG. 3. Nystagmus, again averaged across the 15 subjects, is plotted second-by-second for trials 3 and 8 (the first and last presentation of the interactive stimulus). The terminations of the acceleration are shown by the arrows. Again all data are plotted as geometric means.

second acceleration. While there typically is extensive within and between subjects variability in the duration of primary nystagmic response to a single non-interacting acceleration, a remarkable lack of variability is found in the transition point with interacting stimuli. However, it is evident in Fig. 3 that this transition point shows a slight shift in time consistent with the over-all habituation of the response (16.8 sec to 16.2 sec). Although only the nystagmic responses are plotted, this small shift was evident in both the nystagmic and subjective (16.3 sec to 15.6 sec) transitions for all subjects. It seems reasonable to assume that this shift is a byproduct of the repeated exposure to the interactive stimulus.

DISCUSSION

The present results clearly indicate that nystagmic habituation may occur without nystagmus having run to normal completion. These findings in a situation where there is no period of constant velocity between the interacting stimuli extend and support previous findings that the acquisition of nystagmic habituation is unaffected by the temporal distribution of acceleration experience (Brown 1965, Fearing, 1940, 1941). However distributed experience has been shown to be superior to massed experience relative to the retention of nystagmic habituation (Brown 1965, Fearing, 1940, 1941). A similar effect may well be the case with regard to the retention of habituation to interactive stimuli.

Since the interacting stimuli lead to the occurrence of an abbreviated but yet considerable amount of primary nystagmus to both accelerations, it cannot be concluded that nystagmic habituation is directly related only

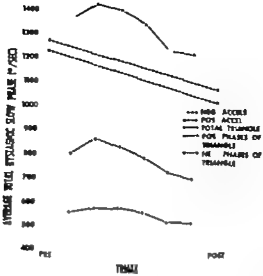

Fig 2 Nystagmus slow phase averaged across responses from the 15 subjects, is pl tted against trial The d shed lines indicate the pre- and post trials while the solid lines indicate the interacting stimuli All data are plotted as geometric means.

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tant dan les réacti d'après-épreuve que dans c lles ux stimuli conjugués, on en a conclu que l'habituation nystagmique peut se produire sans que le nystagmus ne complète son cours normal.

ZUSAMMENFASSUNG

Funfzehn rmale männliche Versuchsperson n wurden wiederholt einer rasch auf inanderf lgenden angularen Beschleunigung unterzogen (iner positiven Beschleunigung, der unmittelbar ine negative Beschleunigung vo gleicher Intensität und Dauer folgte) Vor und nach d n Testen vorgenomm ne Versuch die aus gewöhnlichen einfachen angularen Beschleunigungen besta den, gestatteten d Berechnung der Notwendigk it eine Gewöhnung von Pausen zwischen den nach inander folgenden Stimuli Da bedeutende Abschwachungen bei sowohl den Reaktionen n ch dem Test wie den Reaktionen auf di auf inanderfolgenden Stimuli bemerkt w rden konnte konnt daraus geschlossen werden, dass nystagmische Gewöhnung vorkommen kann ohne das Nystagmus zu einem dadurch bedingten Normalzustand wird

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to the simple repetition of the stimulus Habituation may require the occurrence of only some portion of the total nystagmic potential The present results considered jointly with the findings of Fearing & Mowrer (1934) with anesthetized pigeons, imply that this is the case However a decisive experiment remains to be done since many subjects can completely inhibit nystagmus by fixating a visual stimulus and yet demonstrate habituation equivalent to subjects receiving repeated accelerations in the dark

While subjects exposed to constant angular acceleration in total darkness normally experience no nausea the habituating series in the present study produced some malaise in all subjects Six subjects were replaced after vomiting during the habituating series. Although nausea may occur during angular acceleration when there is concomitant visual stimulation i e visual vestibular interaction (Brown & Crampton 1966 Steele 1963) the present study was conducted in total darkness It is extremely unlikely that head movements are in any way responsible since the subject was belted into the experimental chair and his head was contained in a head rest and further immobilized by a rigid bite board arrangement When necessary an emergency catch allowed the subject to free himself from the bite board It appears that this nausea must be directly related to the interactive stimulus and perhaps should not be too surprising in view of the profound effects upon nystagmic and subjective responses

It should be noted in Fig 3 that interactive effects of the triangular acceleration are exerted not only upon the initial response, where in contrast to normal output a sharply curtailed response is evident but also upon the nystagmic response to the second acceleration Here slow phase output reaches a distinctly sub-normal maximum amplitude clearly below that for the positive acceleration of equal intensity A further effect is that none of the subjects experienced either the normal subjective reversal of direction or a nystagmic phase reversal i e., secondary nystagmus, at the termination of the response to the second acceleration Despite the profound nature of these interactive effects, nystagmic habituation is essentially unaffected Since most non laboratory experience with angular acceleration is of an interactive nature, considerably more emphasis should be placed on the laboratory examination and evaluation of this and similar stimulus patterns

RESUME

Quinze sujets normaux mâles ont été exposés à maintes reprises à les accélérations angulaires conjuguées (c-à-d à la succession continue d une accélération positive suivie d une accélération négative les deux d intensité et de durée égales) Les essais auxquels on a procédé avant et après ces épreuves et qui ont consisté en de simples accélérations standard ont permis une évaluation de la nécessité de s habituer aux intervalles de repos qui arrivaient entre les stimuli offerts successivement Comme des décroissements importants se présentaient

RECRUITMENT IN NOISE-INDUCED HEARING LOSS

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INTRODUCTION

A group of subjects with sensory-neural n ise-induced hearing loss was tested with fixed-frequency Békésy type udiometer Responses were studied for signs f ab ormal auditory adaptatio and increased dif ferential sensitivity Adaptation was defined as a poorer threshold re sponse to continuous ton than t an interrupted ton Increased dif ferential sensitivity was defined as narrower envelope of responses to th continuous ton than to the interrupted tone. It was found that ll subjects showed both of these effects to some degree. It is suggested that adaptation increases differential sensitivity by raising the threshold. It would seem impossible to measure a sensitivity differential unaffected by d ptat on in this category of hearing loss. It is con luded that fi ed-frequency Békésy technique may be the most fruitful approach to recruitment testi g i ce both effects may be measured concurrently with thi procedure

A survey of the literature on recruitment and allied phenomena indicates that there is some disagreement over just what these tests actually measure. Some of the confusion over how to measure recruitment stems from an unclear definition of what it is and disagreement concerning the pathological condition resulting in recruitment. The validity of the tests designed for measuring recruitment is most often questioned. Hirsh, Palva & Goodman (1954) maintain that there need be no relation between recruitment (cochlear pathology) and any difference limen test score On the other hand Dallos & Carhart (1962) feel that increased differential sensitivity (decreased DL size) occurs when there is pathology of the cochlea and that mea urement of the intensity DL in clinical situations can serve as a major diagnostic indicator

Apparently there is unanimous agreement on two points, that the presence of recruitment i compatible with cochlear pathology and that sensory-neural losses resulting from noise exposure exhibit recruitment regardles f the test procedure used (Yantis, 1955) Some investigators use a homogeneous group of subjects with a standard test procedure Other researchers have used heterogeneous gr ups and varied test procedures.

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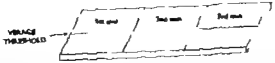

FIG. 1 Average Threshold—Place average threshold line on audiogram so that half the peaks are over the line and half under. Average threshold can then be read from the audiogram.

Average Excursion Width—Count the number of changes of direction of the pen for the time period desired. Then find average excursion width in dB from chart or compute by formula:

Av. Exc. Width

$=$ Time length of tone presentation (sec) $\times$ / No. of excursions

Rate of intensity change

so that very small excursions could be readily differentiated. Data from Chocholle (1942) indicates that reaction time to an auditory stimulus at or near threshold is about 400 ms. The rate of intensity change of the Grason Stadler E-800 is 2 1/2 dB per second or 1 dB per 400 ms. Therefore, the minimum size of any excursion would be approximately 1 dB.

A SISI test was administered to all subjects the same day. A Beltone *Model 15 C* audiometer with a Gordon Stowe SISI Adapter Model 1259 was used.

RESULTS

According to the theory of neural recovery the interrupted or pulsed tone should stimulate normal on-effects in the ear since the rate of 2 1/2 pulses per second allows sufficient recovery time to avoid adaptation (Hallpike & *Hood, 1951*). A poorer threshold for the continuous tone (CT) *than for the* interrupted tone (IT) would indicate adaptation. The magnitude of *such adaptation* under the conditions tested would be apparent from the difference in threshold. Similarly the excursion width of the interrupted tone (IW) could be used as a standard of comparison for the width of the continuous tone excursion (CW). A narrower CW *than IW* would indicate some type of increased differential *sensitivity for the* continuous tone stimulation. The time factor was also important since the *magnitude* of these effects might be expected to vary with stimulus duration.

Average thresholds and excursion widths for both tracings were tabulated for the first and third minutes *only* (see Fig. 2). Threshold means are shown in Table 1 and excursion size means in *Table 2. Differences* between the interrupted and continuous *tone tracings* are shown in Table 3. When the threshold adaptation *occurring during the first minute* is compared with the adaptation during the third minute it will be noted that the greater amount of adaptation occurs during the first minute; only a small additional amount occurs *during the third* minute.

Little has been done however to clarify the recruitment phenomena by studying various facets of one test procedure on one homogeneous group

One test procedure which may be used to detect recruitment is Békésy audiometry The Békésy audiometer has been an invaluable research and clinical tool in the investigation of hearing and in the diagnosis of hearing loss Certain responses and patterns of responses to Békésy audiometry have meaning audiologically A reduction in size of excursion width during the continuous tone presentation has been shown to be related to the presence of recruitment Palva (1957) relates size of excursion width to type of recruitment Other investigators have reported the phenomenon of narrowing of excursion width in cases of noise trauma Data relating to threshold adaptation is less conclusive than that concerning width of excursion

The present investigation proposed to examine exhaustively the responses obtained by means of Békésy audiometry administered to a group of subjects with noise induced hearing losses The testing was limited to timed presentations of selected frequencies

PROCEDURE

Twenty two subjects with a diagnosis of sensory neural noise induced loss were tested A Békésy type audiometer calibrated to ASA (1951) standards (Grason Stadler E-800-4) and equipped with TDH-39 earphones was used for all tests. The subjects received the same directions as for a regular Békésy test and were given a short initial practice period with the pulsed tone After the responses stabilized the test began Using the fixed frequency technique at slow speed ($2\,^1/_2$ dB/sec $2\,^1/_2$ pulses/sec approximately 1 octave/min) five frequencies at octave intervals (500 1000 2000 4000 and 8000 cps) were tested in ascending order Both the pulsed and continuous tones were presented each for a period of three minutes the pulsed tone was presented first in each case The left ear was tested first for half the subjects the right ear for the other half All phases of the testing were completed on one ear before beginning any testing of the opposite ear

Since the variables of interest were stability of threshold and width of the excursion per unit of time a simple device was designed to aid in the measurement of these factors (Fig 1) A thin strip of clear rigid plastic was divided into three segments, each representing the distance the Békésy chart traveled in one minute These divisions made the determination of the number of excursions per minute relatively easy These data were then transformed into average width of excursion in decibels A line along the length of the plastic measuring strip was used to help determine the mid point of an excursion or threshold With this equipment it was relatively easy to obtain the one minute average threshold or excursion size of any tone for any desired minute A recording pen with a fine point was used

TABLE 2. *Average excursion width of continuous and interrupted tones*

Frequency (kc)		Interrupted tone (IW) No. of ears	Mean (dB)	Diff. (dB)	Continuous tone (CW) No. of ears	Mean (dB)	Diff. (dB)
.5	1st min.	43	8.09	−.37	43	8.83	.17
	3rd min.	43	8.46		43	8.66	
1	1st min.	43	8.24	10	43	7.79	.59
	3rd min.	43	8.14		43	7.20	
2	1st min.	43	8.00	− 44	43	6.80	.68
	3rd min.	43	8.44		43	6.12	
4	1st min.	43	8.26	.16	43	5.69	76
	3rd min.	43	8.10		43	4.93	
8	1st min.	22	7.64	05	22	5.25	18
	3rd min.	22	7.59		22	5.07	

TABLE 3 *Threshold and excursion width differences between continuous and interrupted tones*

Frequency (kc)		Threshold differences CT_1–IT	CT_3–IT	Excursion width differences IW_1–CW	IW_3–CW
.5		1.3 dB	1.9 dB	−0.74 dB	−0.20 dB
	SE_D	488		.294	
	t	2.67[a]		−2.41	
1		2.1 dB	4.3 dB	0.45 dB	0.84 dB
	SE_D	470		.273	
	t	4.40[a]		1.66	
2		7.0 dB	9.7 dB	1.20 dB	2.32 dB
	SE_D	.622		.319	
	t	11.22[a]		3.15[a]	
4		7.5 dB	9.6 dB	2.57 dB	3.17 dB
	SE_D	493		.290	
	t	15.17[a]		8.86	
8		9.3 dB	10.9 dB	2.39 dB	2.62 dB
	SE_D	.883		487	
	t	10.46[a]		4.90[a]	

[a] Significant at .05 level.

Note: *t* tests were not performed on 3rd minute differences since the smaller 1st min. differences were significant

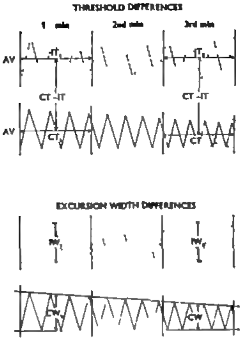

FIG 2 $CT-IT$ = Amount of theshold adaptation of the continuous tone $IW-CW$ = Amount of threshold narrowing of the continuous tone

Table 4 shows the amount of adaptation during the first minute as compared to the cumulative adaptation at the end of three minutes

Thresholds for the group were also obtained by routine manual audiometry Figure 3 records the average thresholds obtained by manual audiometry by the Békésy interrupted tone tracing and by the Békésy continuous tone tracing Interrupted tone thresholds were considerably better for the most part than either manual or continuous tone thresholds

TABLE 1 *Average threshold of continuous and interrupted tones*

Frequency (kc)		Interrupted tone (IT)			Continuous tone (CT)		
		No. of ears	Mean (dB)	Diff (dB)	No. of ears	Mean (dB)	Diff (dB)
.5	1st min.	43	13.6	0.1	43	11.9	0.7
	3rd min.	43	13.7		43	15.0	
1	1st min.	43	22.0	0.3	43	21.1	2.1
	3rd min.	43	22.3		43	20.5	
2	1st min.	43	37.0	0.1	43	41.0	2.8
	3rd min.	43	38.0		43	47.7	
4	1st min.	43	57.3	0.1	43	61.8	2.4
	3rd min.	43	57.7		43	67.2	
8	1st min.	21	43.1	0.3	21	52.1	1.9
	3rd min.	21	43.1		21	51.3	

TABLE 2. *Average excursion width of continuous and interrupted tones*

Frequency (kc)		Interrupted tone (IW) No. of ears	Mean (dB)	Diff. (dB)	Continuous tone (CW) No. of ears	Mean (dB)	Diff. (dB)
.5	1st min.	43	8.09	−.37	43	8.83	.17
	3rd min.	43	8.46		43	8.66	
1	1st min.	43	8.24	.10	43	7.79	.59
	3rd min.	43	8.14		43	7.20	
2	1st min.	43	8.00	−.44	43	6.80	.68
	3rd min.	43	8.44		43	6.12	
4	1st min.	43	8.26	.16	43	5.69	.76
	3rd min.	43	8.10		43	4.93	
8	1st min.	22	7.64	.05	22	5.25	.18
	3rd min.	22	7.59		22	5.07	

TABLE 3. *Threshold and excursion width differences between continuous and interrupted tones*

Frequency (kc)		Threshold differences CT_1-IT	CT_3-IT	Excursion width differences $IW-CW$	IW_3-CW
.5		1.3 dB	1.9 dB	−0.74 dB	−0.30 dB
	SE_D	.496		.304	
	t	2.63[a]		−2.41[a]	
1		2.1 dB	4.2 dB	0.45 dB	0.94 dB
	SE_D	.470		.273	
	t	4.40[a]		1.66	
2		7.0 dB	9.7 dB	1.20 dB	2.32 dB
	SE_D	.600		.349	
	t	11.33[a]		3.43[a]	
4		7.6 dB	9.5 dB	2.57 dB	3.17 dB
	SE_D	.492		.290	
	t	15.17[a]		8.86	
8		[illegible] dB	10.9 dB	2.29 dB	2.82 dB
	SE_D	.883		.467	
	t	10.46[a]		4.90[a]	

[a] Significant at .05 level.

Note: t tests were not performed on 3rd minute differences since the smaller 1st minute differences were significant.

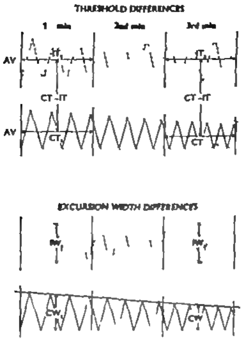

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Table 4 shows the amount of adaptation during the first minute as compared to the cumulative adaptation at the end of three minutes.

Thresholds for the group were also obtained by routine manual audiometry Figure 3 records the average thresholds obtained by manual audiometry by the Békésy interrupted tone tracing and by the Békésy continuous tone tracing Interrupted tone thresholds were considerably better for the most part than either manual or continuous tone thresholds

TABLE 1 *Average threshold of continuous and interrupted tones*

Frequency (kc)		Interrupted tone (IT) No. of ears	Mean (dB)	Diff. (dB)	Contino tone (CT) No of ears	Mean (dB)	Diff (dB)
.5	1st min.	43	13.6	0.1	43	14 9	0.7
	3rd min.	43	13.7		43	15 6	
1	1st min.	43	22.0	0 3	43	24 1	2.4
	3rd min.	43	22.3		43	26.5	
2	1st min.	43	37 9	0 1	43	44 9	2.8
	3rd min.	43	38.0		43	47 7	
4	1st min.	43	57.3	0 1	43	64.8	2.4
	3rd min.	43	5 7		43	67 2	
8	1st min.	21	43 1	0.3	21	52.1	1 9
	3rd min.	21	43.4		21	54.3	

TABLE 2. *Average excursion width of continuous and interrupted tones*

Frequency (kc)		Interrupted tone (IW) No. of ears	Interrupted tone (IW) Mean (dB)	Interrupted tone (IW) Diff. (dB)	Continuous tone (CW) No. of ears	Continuous tone (CW) Mean (dB)	Continuous tone (CW) Diff. (dB)
.5	1st min.	43	8.09	−.37	43	8.83	.17
	3rd min.	43	8.46		43	8.66	
1	1st min.	43	8.24	.10	43	7.79	.59
	3rd min.	43	8.14		43	7.20	
2	1st min.	43	8.00	−.44	43	6.80	.68
	3rd min.	43	8.44		43	6.12	
4	1st min.	43	8.26	.16	43	5.69	.76
	3rd min.	43	8.10		43	4.93	
8	1st min.	22	7.64	.05	22	6.25	.18
	3rd min.	23	7.59		22	6.07	

TABLE 3. *Threshold and excursion width differences between continuous and interrupted tones*

Frequency (kc)		Threshold differences CT_1-IT	Threshold differences CT_3-IT	Excursion width differences IW_1-CW	Excursion width differences IW_3-CW
.5		1.3 dB	1.9 dB	−0.74 dB	−0.20 dB
	$SE_{\bar{D}}$	.486		.304	
	t	2.63[a]		−2.41	
1		2.1 dB	4.2 dB	0.46 dB	0.94 dB
	$SE_{\bar{D}}$	.470		.278	
	t	4.40[a]		1.66	
2		7.0 dB	9.7 dB	1.20 dB	2.32 dB
	$SE_{\bar{D}}$	.609		.349	
	t	11.23[a]		3.43[a]	
4		7.5 dB	9.5 dB	2.57 dB	3.17 dB
	$SE_{\bar{D}}$	.492		.390	
	t	15.17[a]		6.66	
8		9.3 dB	10.9 dB	2.00 dB	2.52 dB
	$SE_{\bar{D}}$	.883		.407	
	t	10.46[a]		4.99[a]	

[a] Significant at .05 level.

Note: t tests were not performed on 3rd minute differences since the smaller 1st minute differences were significant.

TABLE. 4 *Per cent of difference occurring in first minute of tone presentation*

Diff rence between interrupted tone and continuous tone

Narrowing of excursion width (CW)

Frequency	.5 kc	1 kc	2 kc	4 kc	8 kc
Per cent	(*)	48	52	81	85

Worsening of threshold (CT)

Frequency	.5 kc	1 kc	2 kc	4 kc	8 kc
Per cent	68	50	72	79	85

IW was smaller than CW at thi frequ ncy

The SISI scores seemed to be related to degree of hearing loss. Hence correlations (Pearson *r*) were computed between the pure tone threshold and the SISI score for each of the five frequencies (Table 5). The lack of correlation at 4 kc is probably due to the fact that all SISI scores at this frequency were high. Eighty nine per cent of the subjects had scores of at least 8u per cent whereas threshold levels varied over a wide range. As a further check four categories of hearing loss were set up for each frequency: Normal—no greater loss than 10 dB Mild—20 through 30 dB Moderate—40 through 50 dB and Severe—60 dB or greater. Average SISI scores were then computed for each frequency in each category (Table 6). In general the higher the degree of loss the higher the SISI score obtained.

For purpose of comparison several data were plotted on one chart. For ease of comparison each set of data was equated at 4000 cps. From Figure 4 it can be seen that the manual audiometry threshold curve the excursion

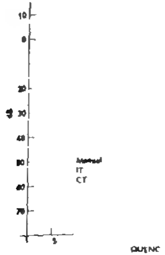

Fig 3. Composit audiogram Mean value f manual audi metry thresh ld, first mi nute interrupted tone threshold and first i inut continuou t ne thresh ld

TABLE 5 *Correlation (Pearson r) between SISI score and hearing level.*

	.5 kc	1 kc	2 kc	4 kc	8 kc
A SISI Sc. (%)	13	40	70	96	[illegible]
A Hear Lc. (dB)	12	24	43	64	41
	.40	.71	.55	.01	.65

Hearing levels in this case were those obtained by manual audiometry.

width difference curve (for the third minute to approximate time required to administer SISI) and the SISI score curve have the same relative shape. The curve representing the difference between continuous and interrupted tone thresholds for the third minute (the adaptation curve) follows a different pattern. For the first three curves there was a steep slope from 500 cps to 4000 cps, at which point a maximum was reached. There was a reversal of direction of slope beyond 4000 cps. Data reported by Riesz (1928) on difference limen (DL) size shows the DL is larger at low frequencies, gets smaller at 1000 and 4000 cps and then increases at 8000 cps. In the present study the curves of increased sensitivity (SISI scores and third minute excursion width difference scores) show the same general tendency. Degree of loss also follows the same general shape. However the curve for adaptation (CT_3–IT_3) is dissimilar in that it continues to rise beyond 4000 cps and reaches its peak at 8000 cps (the highest frequency tested).

TABLE 6 *Average SISI test scores computed according to degree of loss and frequency*

Frequency (kc)	Degree of loss: Normal (%)	Mild (%)	Moderate (%)	Severe (%)
.5	3	35	(*)	(*)
1	4	59	70	(*)
2	(*)	55	91	(*)
4	(*)	(*)	95	97
8	(*)	49	93	99

Normal: Hearing level better than 20 dB.
Mild: Hearing level between 20 and 39 dB.
Moderate: Hearing level between 40 and 59 dB.
Severe: Hearing level 60 dB or greater.
* Insufficient data. Less than 10 per cent of the subjects fell into these categories.

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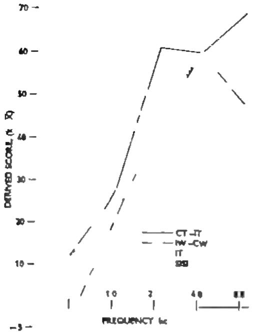

FIG. 4 *CT* − *IT* = Adaptati n of th continuous t n ($k = 6.32$) *IW* − *CW* = Increased sensitivity of the continuon tone ($k = 18.93$) *IT* = Interrupted ton threshold, third minute averag ($k = 1$) *SISI* = Mean SISI score ($k = 0.625$)

DISCUSSION

The experimental data from a sample of military subjects with noise induced losses indicates regular and reliable differences between responses to interrupted and continuous tones The interrupted tone, which would be expected to elicit normal on-effects, shows neither worsening of thresh old (adaptation) nor reduction in excursion width The continuous tone shows a worsening of threshold and a reduction in excursion width which increases with time frequency and degree of hearing loss These effects are apparent not only in comparing the continuous tone to itself over the three minute period but also in comparing it to the interrupted tone The greatest magnitude of change occurs during the first minute of stimulation

These results represent the responses of a sensory neural noise induced group which from the experimental evidence to date should also be a recruiting group Jantis (1955) In his comprehensive survey of recruitment tests, shows that seven investigators found recruitment present 100 per cent of the time in cases of acoustic trauma Therefore the changes in threshold and in excursion width of Békésy tracings may be considered representative of the recruiting ear They illustrate the three main factors of recruitment namely normal on-effect threshold adaptation and increased sensitivity It may be that the lack of reliability of most DL tests is due to the fact that they are only measuring one facet of recruitment—a sensitivity dif

ferential. Dallos & Carhart (1963) conclude that increased differential sensitivity (decreased DL size) indicates cochlear involvement. However the joint occurence of threshold adaptation and increased sensitivity may be even a better indicator

It is hypothesized that with the recruiting ear threshold adaptation must occur before an increased sensitivity may be measured. The effect of adaptation is to worsen the threshold, thereby increasing the stimulus level The higher the stimulus level the smaller is the DL. The present data shows that even manual audiometry is unwittingly measuring the threshold of a partially adapted ear whenever recruitment is present Figure 8 shows this clearly At 1000 2000 and 4000 cps thresholds taken by manual audiometry are identical to those of the adapted ear as measured by the Békésy continuous tone stimulus Yantis & Decker (1964) in their investigation of the SISI test found that as the number of items presented increased (increasing also the time duration of the 20 dB carrier tone) the number of subjects hearing the 1 dB increment also increased They found also that even subjects with high scores (80–95%) missed the increments presented at the beginning of the test This was explained on the basis of the subject s difficulty in making a subjective decision initially as to whether or not he heard the increment. However the present investigators believe that this was due to the fact that adaptation had not yet occurred in the ear Yantis and Decker believe that a high SISI score is in general consistent with the presence of loudness recruitment and end-organ pathology Logically this should follow since the SISI test contains the three elements of on-effect normality adaptation, and sensitivity (even though only one is being measured) If it is true, as Fowler (1950) states, that recruitment is greatest just over the threshold and gradually diminishes with increasing intensity of the stimulation, then the fixed frequency Békésy test may be more conclusi e than the SISI test, since it begins nearer threshold and measures the effect of th weakest conscious stimulus obtainable. Reger & Kos (1952) suggested that all recruitm nt tests at supra-threshold stimulation l vels are contaminated because the high level of stimulation may in itself cause a threshold shift in th recruiting ear Table 1 shows that we may expect average threshold shifts of 10 to 11 dB at 2000 4000 and 8000 cps after a three-minute period of stimulati n and at close to threshold intensities Perhaps this is not a contamination but merely a description of one of the measurable attributes of recruitment.

With the Threshold Tone Decay (TTD) test, Ca hart (1957) noted cases where recruitment and adaptation, at threshold, seem disassociated and that th phenomen n of adaptation (o relapse) seems somewhat independent f other auditory re ctions. Our data shows an daptation effect which is more dependent upon frequency than upon intensity and an increase in sensiti ity which is dependent u pon m unt of hearing loss and intensity of stimulation However both of these effects wer shown by the sam ear in all cases.

Whether or not recruitment is to be defined narrowly as a non linearity of the loudness function with the loudness scale being compressed into a smaller intensity range we would expect the loudness DL to be smaller than normal The narrower width of excursion size of the continuous tone seems to indicate this, whether it is called a reduced loudness DL or a reduced variability (therefore an increased sensitivity) around threshold. In any case the DL is not an absolute value the Weber fraction is constant only in the middle ranges of stimulus values It is actually a measure of the variability of the effects of a stimulus, and in most biological phenomena variability seems to be proportionate to the magnitude of the quantity involved the greater the stimulus, the less the variability The concept of a threshold adaptation occurring first and adding to the effect of intensity on DL size helps to explain the paradox of an ear which is less sensitive threshold wise but more sensitive to small increments of sound

CONCLUSIONS

A group of twenty two subjects with a diagnosis of sensory neural noise-induced hearing loss were tested with Békésy audiometry using the fixed frequency technique All subjects showed some abnormal auditory adaptation and increased sensitivity to intensity change for at least two frequencies Sensitivity (decreased excursion width) increased to a maximum at 4000 cps and decreased at 8000 cps following the Reisz DL data closely SISI scores and hearing level followed the same pattern Adaptation increased with frequency through 8000 cps which was the highest frequency tested SISI scores showed some correlation with hearing level or intensity Hearing levels obtained by routine manual audiometry showed adaptation when compared with Békésy interrupted tone thresholds

The data suggest that adaptation and recruitment are inseparable effects which may be measured simultaneously with fixed frequency Békésy audiometry It is hypothesized that adaptation must first occur before an increased sensitivity to intensity change can be measured and that it is in fact impossible to measure an increased sensitivity (or decreased DL) without adaptation being present It is suggested that for routine clinical use a one-minute period of tone presentation is sufficient instead of the usual three-minute period since most of the difference between the continuous and interrupted tone occurs during the first minute (Table 4)

In regard to the thresholds obtained by manual audiometry it is believed that these are partially adapted thresholds If comparative thresholds are desired it would be necessary to perform manual audiometry using pulsed or interrupted stimuli an ideal pulse rate being 2 $_2$ per second with a duty cycle of 50 per cent (Sergeant & Harris, 1963)

ZUSAMMENFASSUNG

Eine Gruppe von Versuchspersonen mit lärmbedingtem perzeptivem Gehörverlust wurde mit einem frequenzkonstanten Audiometer vom Typ Békésy untersucht. Die Resultate wurden geprüft auf Anzeichen für abnormale auditive Adaptation und gesteigerte Differenzempfindung. Adaptation wurde definiert als schlechtere Schwellenwahrnehmung für Dauerton als für unterbrochenen Ton. Gesteigerte Differenzionempfindung wurde definiert als schmaleres Streuungsband der Messwerte für Dauerton als für unterbrochenen Ton. All Versuchspersonen zeigten beide Effekt in gewissem Masse. Dies lässt vermuten, dass Adaptation di Differenzionempfindung steigert, indem sie di Hörschwelle anhebt. Die Messung eines Empfindungsdifferentiales, unbeeinträchtigt durch Adaptation erscheint bei dieser Art von Hörverlusten unmöglich. Das lässt den Schluss zu, dass ein frequenzkonstante Békésy-Methodik der ergiebigste Weg zur Recruitmentmessung ist, da beide Effekte mit dieser Anordnung gleichzeitig gemessen werden können.

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WEGENER'S GRANULOMATOSIS

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The authors describe the pathological picture in Wegener's granulomatosis and discuss the etiology and pathogenesis of the disease. They report on four cases treated in Helsinki University Otolaryngological Hospital in 1964–65. The disease can be controlled to a high degree by adequate corticosteroid therapy. The authors point out with special emphasis that corticosteroid therapy must be initiated with large suppressive doses. They must be continued until definite healing of the granulating ulcerations is observed. Healing is accompanied by a normalization of the patient's ESR. Subsequently the doses should be gradually lowered until a dose of maintenance level is reached, which in Wegener's granulomatosis varies from case to case and is frequently fairly high. If the maintenance dose is too low, the symptoms recur soon together with a rise in ESR.

Wegener reported in 1936 and 1939 on some cases of fatal granulomatosis of the respiratory tract. The pathological picture of these patients consisted of a destructive granulomatous rhinitis associated with pulmonary symptoms, generalized angiitis and glomerulonephritis. He pointed out that this clinicopathologic syndrome did not apply to any known specific granulomatous disease. He also emphasized the existence of certain similarities to periarteritis nodosa, which as early as 1866 had been described by Kussmaul & Maier. Pathological pictures reminiscent of that described by Wegener had, however, been known before. McBridge had in 1897 reported on a case of rapid destruction of the nose and face. His report was followed by those by Fordyce & Arnold 1906, Woods 1921, Arrowsmith 1921, McArthur 1925, Kraus 1929, Wood 1931, Klinger 1931, Lüdtke 1931 and Hessle 1933. Wegener's report was followed by several publications concerning similar cases: Ringertz 1947, Siirala 1948, Johnsson 1948, Bergqvist & Koch 1949, Ahlström *et al.* 1953, Godman & Churg 1954, Fahey 1956, Paterson 1956, Herberts *et al.* 1957, Walton & Leggat 1958, Blatt *et al.* 1959, Appaix *et al.* 1959, Neuss 1960, Brown & Woolner 1960, Ludman 1963, Beidleman 1963, Escher & Legrain 1963, Zechner 1963, Friedmann 1964, Mills 1964, Ardouin 1964, and Lehnhardt 1964.

Wegener's granulomatosis has a typical history and a fairly typical clinical course. The disease can be divided into three phases: the prodromal

phase, the phase of the active disease, and the terminal phase During the prodromal phase there are, sporadically at first, small non-typical lesions in the mucosa of the nose and mouth. The sores heal but after a time fresh ones develop During the active phase of the disease granulating necrotic lesions are seen mostly in the upper and lower respiratory tract. There are gradual pathological changes in the kidneys. The terminal phase often ends with a destructive process in the upper respiratory tract which leads to death, due to massive infection and toxin resorption or arrosion bleeding Sometimes a lingering death is caused by pulmonary and renal processes. The nephrosis finally results in uremia

Godman & Churg (1954) listed the pathologic characteristics of Wegener's granulomatosis as follows (1) A necrotizing granulomatous process involving the upper or lower part of the respiratory tract or both. (2) Generalized focal necrosing vasculitis involving both arteries and veins, almost always in the lungs and more or less widely disseminated in other tissues. (3) Glomerulitis characterized by necrosis of loops or lobes of the capillary tuft adhesions and development as a granulomatous lesion

Etiology and pathogenesis

Wegener's granulomatosis shows many features seen in hyperergia or hypersensitivity In hyperergia the patient's immunity reaction is disturbed If allergy is given a wide meaning hyperergia can be included in this concept. The antigen-antibody combination is also present in hyperergia. In allergy in the more restricted sense of the word, the reactivity of the tissues has changed qualitatively whereas in hyperergia the change is quantitative and the reaction often follows slowly leaving permanent traces. These permanent pathological changes in the tissues of the host organism are typical of hyperergia.

The mechanism producing the first tissue damage is not known with certainty It is possible that, in chronic infection of the respiratory tract, damaged tissues or proteins of the body are liberated and may later be felt to be extraneous by the organism. In this way they can provoke autoantibody formation. Antigen-antibody reaction follows, leading to a fresh tissu lesion, which liberates new antigens, and so a vicious circle is started In Weg ner's granulomatosis antigen-antibody reaction centres in the respiratory tract It is a known fact that the mucosa of the respiratory tract is disposed to local sensitization. The present authors views on the etiology and pathogenesis in Wegener's granulomatosis are described in another paper (Zechner & Grahne, 1965)

Therapy and prognosis

Corticosteroid therapy has proved effective in Wegener's granulomatosis But it i important to know that the course of the disease can be controlled only with initially large, suppressive doses The literature also reports the complet failures of corticosteroid treatment. It is obvious, however that

in these cases the dosage, especially the initial dosage has been far too small The prognosis *quo ad vitam* is poor although the patients can often manage to live for years with adequate corticosteroid therapy

Differential diagnosis

It must be assumed that Wegener s granulomatosis and the so-called lethal midline granuloma which has perhaps been best described by Stewart (1931) are somewhat similar conditions Periarteritis nodosa may also be considered another form of the same disease

Lymphosarcoma and reticulosarcoma may also exactly reproduce the clinical features of nonhealing granuloma of the nose Biopsy specimens from early lesions, particularly may be difficult to distinguish from Wegener s granulomatosis The distinction between tumour like proliferative diseases and true neoplasms is nowhere less clear than in the lymphoreticular system (Symmers, 1958 Friedmann 1964) Friedmann (1964) wondered whether the nonhealing granuloma of the nose in some instances might not be the precursor of these neoplasms He says that one talked of precancerous lesions, but could one suggest a presarcomatous lesion?" In the cases described below the problems mentioned by Friedmann were however not met

Report of cases

The four cases to be described below were all treated in 1964–65 at the Helsinki University Otolaryngological Hospital The authors wish to emphasize that the course of the disease could be influenced to a high degree by adequate corticosteroid therapy

Case 1 Female aged 24 years.

The patient had had menarche at the age of 18 but had menstruated only 5 times before menstruation discontinued She had noticed the first lesions in the oral mucosa 9 years previously but they had healed soon Subsequently there had been sporadic lesions in the mouth For 6 years she had had permanently suppurating, necrotic lesions in the mucosa of the mouth pharynx and larynx She had been treated 6 years previously at a tuberculosis sanatorium for suspected non verifiable laryngeal tuberculosis At the same time the patient had sores in the anal tract and in the urethral mucosa her ESR was 0 mm Hg/h Four years ago her AST was 100 and ASTA 4 and the gammaglobulins in paper electrophoresis were 31 7 per cent The patient had sporadically been given small doses of corticosteroids, together with antibiotics, but the lesions in the respiratory tract had refused to heal A year ago changes reminiscent of bronchiectasis were found in both lungs, and microhaematuria

The patient was admitted to Helsinki University Otolaryngological Hospital in August 1964 for examination She was found to have suppurating necrotic lesions in the respiratory tract and a phlegm producing cough In October he was given a subcutaneous injection of atropedin (Pethidin chlorid + atropine sulph + phenylcarbinol) in one arm Immediately her whole body was covered by an urticarian exanthema and her head mouth and nose became oedematous.

Fig. 1. Case 1. Subepithelial granulation tissue with numerous blood vessels and few fibres. ×200. Nasal vertical m st in.

Due to laryngeal and bronchial swelling she had severe dyspnea. A large fluid filled bulla developed at the site of injection. Corticosteroid treatment with large suppressive doses was started immediately (12 prednison tablets 5 mg each per day) while antibiotics were also given. Dramatic improvement of all symptoms followed in a few days. The lesions in the mouth, pharynx and larynx showed a distinct tendency to heal. After a fortnight of high suppressive cortison dosage the dose was gradually reduced. About 3 weeks from the start of cortisone treatment all the lesions had healed. The ESR fell in these 3 weeks from 66 to 8 mm Hg/h. The patient is now relatively symptom-free on a maintenance dose of 3 tablets of prednison daily. It may be mentioned that the patient, after the symptoms had disappeared and the maintenance dose of prednison established, was given another injection of tropedin of the same strength as had previously produced such severe allergic symtoms, but this injection produced no reaction.

Case 2. Male aged 27 years.

In 1946 the patient noticed sporadic lesions in the mucosa of the mouth, some of them the size of the nail of the little finger. At the same time there were sores around the anus. To start with, the lesions healed from time to time but were replaced by fresh ones. Freedom from symptoms lasted at first for a maximum of a month. Since 1953 the lesions in the mouth, pharynx, and larynx no longer healed. The patient's voice had also been hoarse since 1955. Time and again there had been lesions on the scrotum and penis. Occasionally the patient had had urticarious exanthema on the neck and legs, but it had soon disappeared. His ESR had mostly remained at about 50 mm Hg/h. He had had a cough with phlegm formation for many years, and when younger he had often had angina. In 1962 he had pneumonia. He had been treated on several occasions at different hospitals for his lesions. The diagnosis varied from hospital to hospital. He had sporadically been given small doses of corticosteroids without any distinct benefit. He was admitted to the Helsinki University Otolaryngological Hospital in January 1963 with extensive deep necrotic ulcerations in the mouth, mesopharynx and larynx. Thorax x-ray revealed peri-

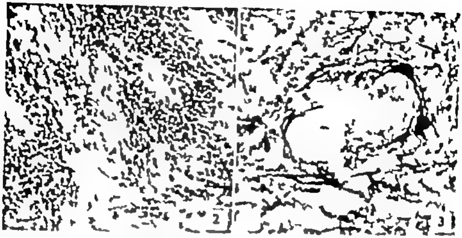

Fig. 2. Case 2. Scars interspersed with infected granulomas. ×200. van Gieson stain.

Fig. 3. Case 2. Vasculitis with fresh thrombi. Clotted fibres. ×400. Nassar reticulum stain.

bronchitis and traces of earlier pleurisy. ESR on admission was 16 mm Hg h. Microscopy of urinary sediment revealed a few erythrocytes in each field of vision. Paper electrophoresis of the serum showed a slight elevation of gamma globulins (19.2 per cent). Immunoelectrophoresis revealed a slight elevation of γ-A globulin. Corticosteroid therapy was initiated with 16 tablets of dexamethasone 0.5 mg each daily. A definite healing process of the lesions was visible in a few days. After 4 days the dose was reduced to 10 tablets and after another 4 days to 6 tablets daily. The maintenance dose for this patient was 4 tablets of dexamethasone 0.5 mg each daily. It has been noted that as soon as the maintenance dose is less than 4 tablets daily the symptoms recur immediately. The patient is now practically free of symptoms but has continuous microhematuria.

Case 3. Male, aged 61 years

The patient had been generally healthy until 1961 when he began to complain of pain on deep inhalation. Thorax x-ray films revealed tumour-like shadows in the basal part of the right lung. At the same time radiography also revealed gallstones. The patient had a cough with phlegm formation and fever for 3 months. Radiography showed that the tumour-like infiltrates spread higher and higher in the lung tissue. Right pneumectomy was carried out in the autumn of 1961, followed in 3 months by a gallstone operation. The patient recovered surprisingly rapidly after both operations. Histopathological examination of the lung tumour revealed a benign process. The patient was subsequently in good health until May 1964 when his right cheek gradually began to swell. The swelling was accompanied by pain. After a few weeks he began to see double. The right maxillary sinus was operated on at a local hospital in June 1964 using Caldwell-Luc's method. An oromaxillary fistula as wide as a finger developed postoperatively in the incision line. According to the operation report the maxillary sinus was filled with tumour-like tissue. In August 1964 the right cheek swelled again and pain returned. Another Caldwell-Luc operation was performed with extirpation of the tumour tissue which again filled the whole

Fig. 4 Case 3. Arteritis from the lung. Infected wall infiltrates. 200 × an Olesso stain

Fig. 5 Case 3 Complete loss of fibres in the inner wall layers. 400 × Nassa reticulum stain.

ma illary sinus. However the sinus wa soon refilled by fresh tumou tl sue. An oromax llary fistula 3 cm in diameter remained after the operation. The diagnosis f Wege er' granulomatosis was not made until January 1963. A reexamin tion f the specimen taken at pneumectomy d th earlier m xillary sinus operations revealed histological changes typical of W gener' granulomatosis. Serum lectrophoresis revealed elevated gammaglobulin level (23 per ent). Immunoelectrophoresis showed th t the values for gammaglobulin γ-A and γ 2 G/A globulin w re elevated. Microscopy f the urinary sediment revealed microhematuria. ESR w 94 mm Hg/h. Corticosteroid therapy with suppressive doses wa begun. To start with, the patient was given 16 tablets of dexamethason 0.5 mg each daily. After 2 days a marked regression f symptoms was noted. The corticosteroid dose was reduced after 5 day t 9 tablets daily and after nother 8 day to 3 tablets daily. I 17 days the ESR f ll from 94 to 11 mm Hg/h. The maintena ce dose fo thi patient was found to be 4 tablets of dex methasone 0.5 mg ea h daily. W th this dose the pati t has been practically ymptom-free.

Case 4. Mal aged 51 years.

The patient had been generally healthy until 1933 when hard crimson infiltration began t ppea on the skin of his lower abdomen. At the same time he contracted slight nephritis which has persisted eve since. Subsequently crimson infiltrates occasion lly ppeared n th abdomen and on the rms. They healed gradually but were replaced by ew infiltrates i other parts of the skin. In 1938 biopsy specimen were taken from the infiltrates f h stological xamination. Th path logist mad the f llowing statement: The epidermis was ormal. I th subcutis of both veins and arteries there were chron i flammation cell i the media and adventitia. Th hanges were remi iscent of those in thromboa giitis obliterans. Periarteritis nodosa could not be excluded, but the fact that cha ges occurred both in the arteries and ein was gainst this assumption. U inary sediment showed 1 3 erythrocytes

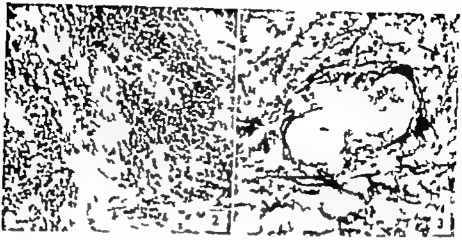

Fig 2 Case 2 Scars interspersed with infected granuloma ×200 van Gieson stain

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tween the physician and the pathologist is required. The histopathological changes may be difficult to interpret. It may not be easy to distinguish the vascular changes, for example, from those seen in necrotizing infection

It has been shown above that Wegener s granulomatosis can be controlled by corticosteroids. It must be particularly emphasized that the dosage must be suppressive. No results are achieved if treatment starts with small doses and is increased gradually This method was tried in Case 4 where a 6-week treatment had no effect on the granulation process Only after a suppressi e dosage introduced did the patient respond, in a few days The ESR seems to indicate clearly whether or not the dose is adequate correct dosage normalizes the ESR in a few days. Dexamethasone was employed in all cases except Case 1 since it is considered to have a smaller mineral steroid effect than prednisone and prednisolone which perhaps are the most gener ally used corticosteroids. On the other hand, dexamethasone is believed to paralyse more easily the adrenal cortex function. Our argument was that this adrenal cortex function will be destroyed in any case, since a relatively high maintenance dose of corticosteroids is given over a prolonged period For this reason no ACTH therapy was introduced in these cases. Antibiotics were given only in the initial phases of corticosteroid therapy but once the necrotic process had rapidly healed the antibiotics were suspended. Anti biotics, together with a somewhat increased dose of corticosteroids, have been recommended for temporary use in the event of any future bacterial infection

Wegenner's granulomatosis evidently requires a relatively high main tenance dose of corticosteroids. In Case 1 of the present series the maintenance dose was 3 tablets of prednisone 5 mg each per day In Cases 2, 3 and 4 the daily dose was 4 4 and 8 tablets of dexamethasone 0.5 mg each Any reduction of the maintenance dose in these cases at once resulted in an ulcerative granulation process in the healed cicatricial tissue and in an elevated ESR It is also striking how the adequate maintenance level protected Case 1 against exanthema when the patient was subjected to the sam antigen exposure, which prior to cortisone th rapy was fol lowed by violent course of exanthema, swelling, and a bulla at the site f the injection.

Th general opinion has been that surgery in Wegener's granulomatosis results in the process flaring up swiftly with tissue destruction leading to death It is interesting to see that one of th present patients (Case 3) was subjected to pneumectomy and a gallstone operation without corticosteroid therapy and his operation wound healed without the process flaring up B t in this case the incisions did not penetrate the necrotic granulation ti e Th s same patient underwent two Caldwell–Luc operations in which th ffected tissue was incised. The pathological process flared up and a la ge oroantral fistula wa formed, but death did not follow The patient later had nother operation in which the large oroantral fistula was obturated This time surgery was performed under protection of the patient s

FIG 6 Case 4 Subepithelial mixed and infected infiltrates. ×200 van Gieson stain.
FIG 7 Case 4 Fibrous swelling in a focus of fibrinoid necrosis. ×600 Wilder reticulum stain

per field of vision Cerebrospinal fluid contained 44 leucocytes of which 72 per cent were lymphocytes and 28 per cent granulocytes Incipient progressive loss of hearing was noted towards the end of 1959 In 3 months the loss of hearing of the left ear was total Towards the end of 1961 the hearing of the right ear began to weaken and 3 months later the loss was total There was no discharge from the ears and no vertigo Explorative antrostomy was performed in 1963 on the right ear the antrum aditus and the pneumatic cells were found to contain granulation tissue No histological examination was performed Since 1953 the patient's LSR had remained at around 100 He had sporadically been given small doses of corticosteroids and had felt slightly better In February 1965 the patient was admitted to Helsinki University Otolaryngological Hospital with an ulcerating necrotic granulation process in the nasal septum He had microhematuria and his ESR was 112 mm Hg/h Corticosteroid treatment was started in this case experimentally with fairly low dosage which was to be increased gradually until response was obtained This method however failed to give results. The granulation process was not affected nor was the LSR despite the fact that the dose gradually increased to 8 tablets of dexamethasone 0 5 mg each daily It was then decided to reverse the treatment and give the patient large suppressive doses For 8 days he was given 16 tablets daily of dexamethasone 0.5 mg each This affected the granulation process almost immediately The dose was gradually reduced until a maintenance level of 8 tablets daily was reached ESR fell in 14 days from 11 to 34 mm Hg/h Microhematuria remained unchanged in this patient also His general condition improved remarkably The granulation process of the nasal septum disappeared completely leaving a perforation the width of a finger with smooth edges.

DISCUSSION

All the cases described above can be classified under the diagnosis of Wegener's granulomatosis To obtain the diagnosis good cooperation be-

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customary maintenance dose of dexamethasone without increasing the dose. The site of operation healed well.

The authors consider that lethal midline granuloma (type Stewart), Wegener's granulomatosis and periarteritis nodosa are different forms of the same pathological process. The dissimilarities are largely in the different location of the processes. Lethal midline granuloma is the most localized type, although necropsy may show in these cases that the pathological changes are also present in other parts of the body, as is the case in Wegener's granulomatosis. The most widespread are the changes in periarteritis nodosa, of which the clinical picture can occur simultaneously in Wegener's granulomatosis (Case 4). It may be assumed, perhaps, that the antigen in lethal midline granuloma (type Stewart) and in Wegener's granulomatosis affects the organism via the respiratory tract while in periarteritis nodosa the antigen may be assumed to be carried by the circulating blood.

ZUSAMMENFASSUNG

Die Verfasser beschreiben das Krankheitsbild der Wegenerschen Granulomatose und besprechen auch die Ätiologie und Pathogenese der Krankheit. Sie berichten über vier Fälle, die an der Universitäts-Ohrenklinik in Helsinki in den Jahren 1904–1905 behandelt worden sind. Die Krankheit kann weitgehend mit adäquater Kortikosteroidbehandlung beeinflusst werden. Die Verfasser heben besonders hervor, dass die Kortikosteroidbehandlung mit grossen suppressiven Dosen eingeleitet werden muss. Die Behandlung mit diesen grossen suppressiven Dosen muss so lange fortgesetzt werden, bis eine deutliche Heilung der granulierenden Ulzerationen wahrzunehmen ist. Im Gefolge dieses Heilungsprozesses sinkt dann der Blutsenkungswert auf normale Höhe. Danach soll die Dosierung allmählich vermindert werden, bis man die Erhaltungsdosis erreicht hat, die bei der Wegenerschen Granulomatose von Fall zu Fall verschieden und nicht selten ziemlich gross ist. Wenn die Erhaltungsdosis zu klein ist, stellen sich die Symptome bald wieder ein, während zugleich die Blutsenkung wieder ansteigt.

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ACOUSTIC INPUT IMPEDANCE OF THE HUMAN EAR

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An objective method of measuring the vibration of the tympanic membrane by means of an improved capacitive-probe system is described. The device has a dynamic range up to 7000 Å over the whole audio-frequency range. A new probe tip was developed, serving for conduction of the modulated H.F. signal as well as for the sound transmission. The acoustic input impedance of the ear of 1 fresh temporal bone preparations was evaluated over the whole audio frequency range and comparisons between the unloaded and the ear loaded by the inner ear were made. Characteristics of the ear were obtained from these data.

INTRODUCTION

There are several approaches to the study of the mechanical impedance of the human ear. Some are based on absolute acoustic input impedance measurements, others use the relative method.

Troeger (1930) made use of the reflection method for measuring the acoustic impedance. In addition to the information regarding energy absorption by the ear, his method revealed the phase relation between the applied wave and the reflected wave, thus determining the reactance of the ear. Troeger's study was carried out at specific frequencies in the range 250–3000 cps. His method is subject to large experimental errors.

Waetzmann (1938) employed the acoustic bridge for measuring the input impedance of the ear. It was measured at discrete frequencies by comparison with a standard impedance. The principal difficulty of this method is that suitable variable standards of acoustic resistance and reactance have not yet been developed.

Recently the relative acoustic input impedance of the ear was introduced by Metz (1951) and by Moeller (1961). Contraction of the middle ear muscles produces a change in the acoustic behaviour of the ear's sound conducting system, which can be measured as a change in the acoustic impedance. Where the acoustic reflex cannot be elicited (e.g. in the case of otosclerosis, ossicular interruption, adhesive otitis etc.) diagnostic differentiation between middle ear pathologies is very difficult, due to the similarity between the results in the above cases.

The work presented here describes another absolute method based on measurement of the vibrations of the tympanic membrane and consequently

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Waetzmann (1938) employed the acoustic bridge for measuring the input impedance of the ear. It was measured at discrete frequencies by comparison with a standard impedance. The principal difficulty of this method is that suitable variable standards of acoustic resistance and reactance have not yet been developed.

Recently the relative acoustic input impedance of the ear was introduced by Metz (1951) and by Moeller (1961). Contraction of the middle ear muscles produces a change in the acoustic behaviour of the ear's sound conducting system, which can be measured as a change in the acoustic impedance. Where the acoustic reflex cannot be elicited (e.g. in the case of otosclerosis, ossicular interruption, adhesive otitis etc.) diagnostic differentiation between middle ear pathologies is very difficult, due to the similarity between the results in the above cases.

The work presented here describes another absolute method based on measurement of the vibrations of the tympanic membrane and consequently

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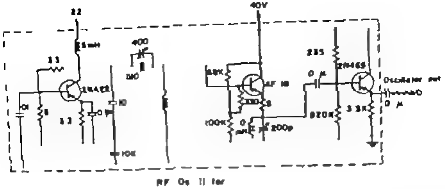


FIG. 2.

allows determination of the acoustic input impedance of the ear. This has the advantage of being objective, and of allowing repeatable and accurate measurements to be made over a wide frequency and dynamic range. The measurement can also be completed in a short period of time.

METHOD

A. Measuring Device

The work presented here is based on measurement of the absolute acoustic input impedance of the ear by means of a capacitive probe vibration meter. The measurement of vibrations (order of magnitude 10 Å) is accomplished by measuring the changes of the capacity which consists of the plate of the probe and the vibrating part (Rubinstein *et al.*, 1964). The measuring device is an advanced development of a previously reported apparatus (Fischler *et al.* 1964). The improvements result is a more universal device. Some electronic and constructional changes were introduced to improve the performance of the device.

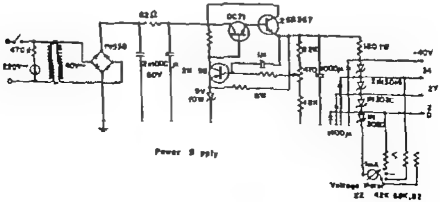
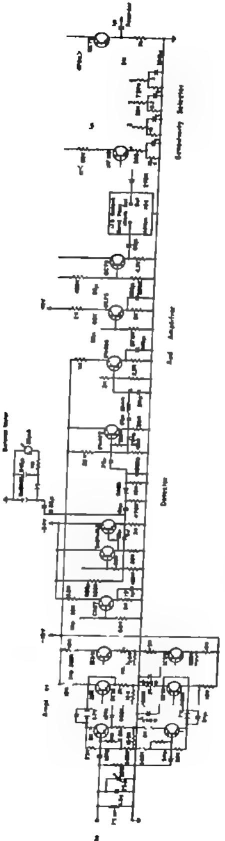


FIG. 3.



Figs. 1 3 Circuit diagram of capacitive-probe vibration met r

Fig 1

The advantage of our device lies in its wide dynamic range, so as to include vibrations excited by a sound level up to 124 dB even in cases of good mobility of the membrane The apparatus enables measurements in the whole audio frequency range to be made by continuous automatic recording, within 3 minutes. In contrast to other absolute methods this system need not consider the air column between the probe and the tympanic membrane The testing frequency can serve simultaneously for stimulation of muscle reflexes and for measuring the tested ear itself

MEASUREMENTS

Experiments were made on 15 fresh temporal bone preparations in order to find characteristic patterns of the ear impedance as a function of frequency and its dependence on anatomical structure Another purpose was to find the relation between the characteristic curve of the middle ear loaded by the inner ear and the curve obtained after removal of the cochlea. This was achieved by extraction of the temporal bone together with the inner ear the study of the tympanic membrane vibrations, the removal of the inner ear and further measurement of the vibrations of the tympanic membrane The vibrations of the stapes were also recorded simultaneously During this procedure steps were taken to keep the preparation fresh by preserving it in a refrigerator and moistening it with physiologic solution.

RESULTS

The results of the measurements are given in Figs 4–9

(1) In spite of the differences in frequency characteristics of the various temporal bone preparations, it appears that in all cases the hearing system contains three regions of relatively high sensitivity separated by rather harp drops in the higher frequency region. At lower frequencies the h racteri tic curve increases gradually These features are even more emphasized in the acoustic input impedance curves three resonance points appear in the region of higher frequencies, while at lower frequencies the impedance decreases gradually with increasing frequency and is accompanied by small ondulations. (These results were obtained for all preparation examined except that the gradient of the acoustic input impedance urves in the low frequency region shows some variations.)

The regions of the first acoustic impedance resonance appears systematically between 1000–2000 cps and is relatively broad. The second impedance appears at about 500 cps, and the third at about 800 cps.

\ c mparison f the frequency characteristics of the preparations Figs. 4 9 examined shows, that apart from mall changes in the location of the resonances, they are essentially of the same shape and differ only with

The following improvements are of significance

(1) Selection of the displacement amplitude range in four successive steps makes it easy to cover a large excitation sound level range This was accomplished by changing the gain of the last audio stage (Fig 1) Exact calibration of the amplifier is needed in order to achieve a correspondance of the displacement to a certain output voltage This was performed with the Goodman s Vibration Meter (Model V47)

(2) An electronic distance meter was incorporated as a separate channel to indicate the distance between the capacity probe face and the measured area The distance measurement is accomplished by detection of the RF signal and D-C metering Thus the use of an auxiliary oscilloscope is avoided

(3) The last stage of the HF amplifier is a Darlington Circuit" serving as a matching element between the last HF amplifier stage and the parallel branches of RF detector and distance meter (Fig 1)

(4) In order to achieve load independence of the RF Oscillator output voltage a buffer stage following the L-C filter of the oscillator was built (Fig 2)

(5) The stabilized power supply (Fig 3) replaces the previous one

A new probe tip was developed It consists of a hollow tube (1.5 mm) along the axis of which a cupper wire (0 1 mm) is streched with a silver plate of 2 mm diameter at one end and a screened coaxial cable (0 8 mm) at the other end This probe has a dual function as a capacitive probe conducting the modulated signal to the HF amplifier and as a sound pressure probe conducting the sound waves to the sound level control microphone *The advantage of this probe lies in the precision of measuring the sound pressure always at the same distance from the vibrating area*

The specifications of the vibration meter are at present as follows (*a*) *Measuring ranges* 2.5 5 10 25 Å for 0 dB of the recorder Range selection by switch (*b*) *Dynamic range* up to 7500 Å (*c*) *Frequency range* 20—20 000 cps (*d*) *Internal noise* The noise frequency curve has a maximum of 5 dB $\hat{=}$ 45 Å (0 dB $\hat{=}$ 25 Å) at 3000 cps and falls towards 0 dB at both ends of the frequency range

B *Evaluation*

The acoustic input impedance of the ear is determined from the recorded displacement curve as function of frequency of the tympanic membrane at the umbo for constant sound levels The corresponding formula is (Fischler *et al*)

$$Z(\text{dB}) = P(\text{dB}) - D(\text{dB}) - 20 \log(2\pi f)$$

where Z = acoustic input impedance, P = sound pressure D = displacement f = frequency

The advantage of our device lies in its wide dynamic range so as to include vibrations excited by a sound level up to 124 dB, even in cases of good mobility of the membrane The apparatus enables measurements in the whole audio frequency range to be made by continuous automatic recording, within 3 minutes In contrast to other absolute methods, this system need not consider the air column between the probe and the tympanic membrane The testing frequency can serve simultaneously for stimulation of muscle reflexes and for measuring the tested ear itself

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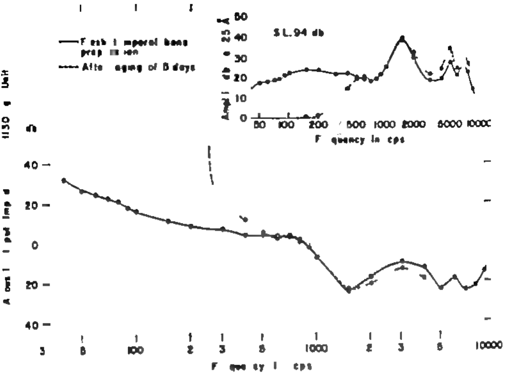
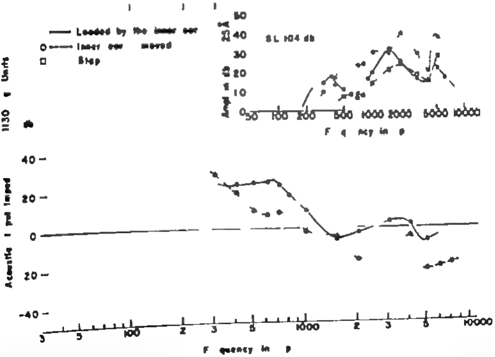


Fig. 4. Acoustic input impedance characteristic of a fresh temporal bone preparation and the same preparation after 8 days aging.



Figs. 8–9. (1) Acoustic input impedance characteristics of temporal bone preparations, measured at the umbo: (a) loaded by the inner ear; (b) inner ear removed; sound level: 104 db. Corresponding displacement curves: (a) of the tympanic membrane at the umbo, and (b) of the stapes.

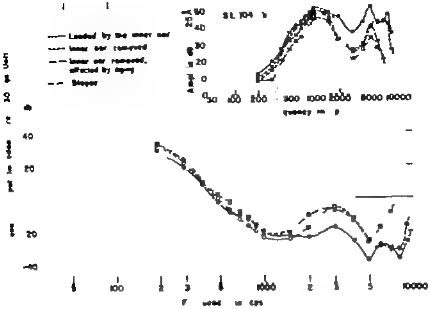


FIG. 6.

respect to the amplitude A physiological examination of these preparations revealed no anatomical abnormalities. In contrast we see that there exist remarkable deviations in the form of frequency characteristics of pathological temporal bone preparations, e.g. at an otosclerotic ear (Fig 10 in Fischler et al., 1966)

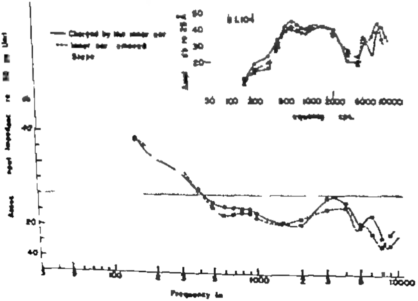


FIG. 7

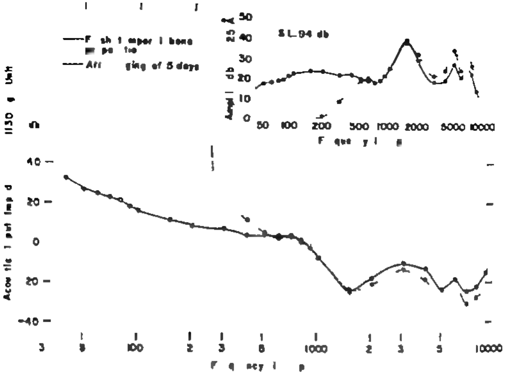
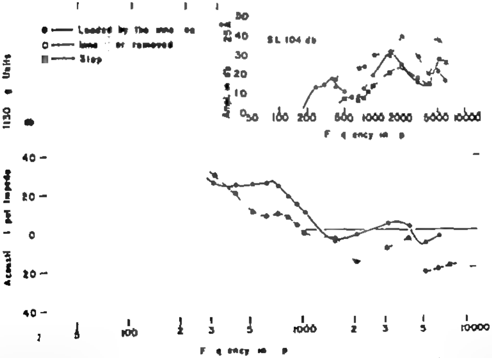
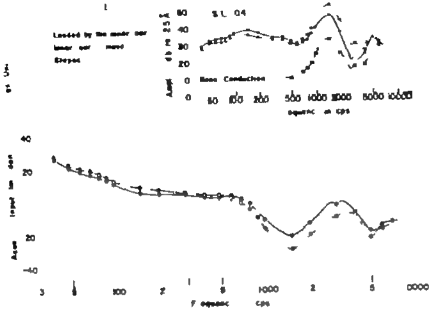


Fig. 4. Acoustic input impedance characteristic of a fresh temporal bone preparation and the same preparation after 5 day aging



Figs. 5–9 (1) Acoustic input impedance characteristics of temporal bone preparations, measured at the umbo (*a*) loaded by the inner ear (*b*) inner ear removed sound level 104 db. Corresponding displacement curves: (*a*) of the tympanic membrane at the umbo, and (*b*) of the stapes.



F a. 9.

are not all on the same level They tend, with increasing frequency towards the minimum level mentioned. It is assumed that there exists another real resistive component determined by the mechanical structure of the ossicles which is frequency dependent. This phenomenon may be characteristic to cadaver preparations, as a result of aging

(1 *b*) The locations of the acoustic impedance resonances fit closely to those of Lawrence (1950) (even though cats were used in his work) From th phase-frequency curve appearing in that article it can be seen th t the locations of the ear's sensitivity peaks correspond closely with the frequencies at which the phase changes its sign.

(2) Th phenomenon of resonance-frequency shift, resulting from removal of the inner ear as i shown n the impedance curve, can be explained by a mass decrease due to removal of the cochlea load

(3) The pread in magnitude of the lever transformation ratio as a function of frequency and for varion temporal bones, is explained by its dependence on the degree of mobility of the ossicle chain and especially f the tapedial footpl te

(4) Reduction of low frequ ncy sensitivity observed in the aged anatomical preparation, is caused by increa ing stiffness of the ossicular chain.

Of the anat mical structure involved in the drying p ocess, by far the most importa t part i the annular ligament of the stapedial footplate.

A imilar occ rrence of sen itivity decrease at low frequencies can be seen in the udiometric test of early otosclerotic cases where the otosclerotic focu just begin to i filtrate the annular ligament.

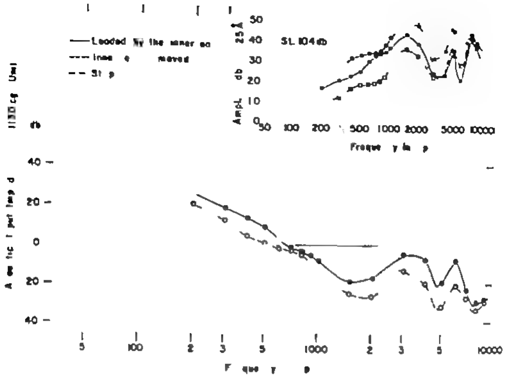


Fig. 8.

(2) Comparing the impedance curve of the same temporal bone preparation before and after removal of the inner ear it can be seen that (taking into account the aging of the preparation and the influence of the cutting procedure on aging) there is a decrease in the acoustic impedance after operation We also note in some of the preparations a remarkable shift of the resonances

(3) Measuring the vibrations of the tympanic membrane and of the stapes simultaneously enables us to evaluate the lever transformation ratio of the unloaded middle ear ossicles throughout the frequency range This ratio shows a great spread for differing frequencies and for different preparations, while the shape of the frequency curve for the stapes is preserved

(4) The effect of aging of the preparation can be seen in Figs 4 and 6 This natural process is revealed by an increase in the acoustic impedance which becomes more pronounced in the lower frequency range

DISCUSSION

(1 a) By comparing the acoustic input impedance of the unloaded ear preparations (Figs 4–9) it can be seen that the three resonance points have (within the limits set by errors of measurement) a value coinciding closely with the characteristic impedance of air which is 41.5 dyn sec cm $\triangleq$28 7 dB This evidences optimal matching of the middle ear to the air at these points Some above-mentioned results show that those resonances

gangsimpedanz des Ohres von 15 frischen Postmortem-Präparaten wurde über den ganzen Tonfrequenzbereich verwertet, und Vergleiche zwischen dem unbelasteten und dem mit dem Innenohr belasteten Ohr wurden gezogen. Die Ergebnisse gaben Aufschluss über das charakteristische Verhalten des Ohres.

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CONCLUSION

(1) The main importance of the acoustic impedance curves for the whole reconstructive surgery of the ear[1] lies in the possible evaluation of the "cochlear reserve" (i.e. the functional value of the inner ear and the supra cochlear pathways) by a more reliable method

The conventional audiometric examination uses air and bone-conducted sounds The air conduction test provides information on the sensitivity of the whole hearing system The bone conduction test, by passing the middle ear is supposed to measure the loss due to neural pathology only (i.e. cochlear and supra cochlear defects) The difference between those two factors gives the loss due to the middle ear pathology This value is the basis of surgical treatment of middle ear diseases Unfortunately this procedure does not always give the desired result This is due to uncertainty in the reliability of the bone conduction test which is often influenced by the middle ear pathology (e.g. Shambaugh-Carhart notch, Weber lateralization in conductive hearing loss absolute bone conduction etc.)

Contrary to the conventional audiometric technique it may be possible with the method described in this article, to determine the sensitivity loss caused by a defect in the inner ear with far better reliability

With the conventional method of hearing examination it is not possible to determine the functional value of the inner ear in the frequency range above 4000 cps due to the limitations of the mechanical vibrator (bone conductor) Such a limitation does not exist in our method

(2) The acoustic input impedance curve is dependent on the structure of the conductive system Comparison between the impedance curve of the examined ear and that of a normal one may therefore supply information about the pathology of the middle ear Differences in the shape of the *impedance curve may lead to conclusions about the specific pathology* of the middle ear while the absolute impedance values may be an indicative examination of the degree of deafness

ZUSAMMENFASSUNG

Es wird eine Methode beschrieben für objektive Messung der Vibrationen des Trommelfells mit Hilfe eines kapazitiven Sondensystems. Das Instrument hat über den ganzen Tonfrequenzbereich einen dynamischen Bereich bis zu 7000 Å. Eine neue Sonde wurde entwickelt, welche gleichzeitig zur Leitung des modulierten H.F.-Signals wie auch fur die Tonführung dient Die akustische Ein

[1] In trying to apply this method clinically difficulties arise due to the small distance between the tympanic membrane and the probe Spontaneous movement of the patient's head might cause damage to the membrane We are considering means to solve this problem.

Table 1 *Method and optimum exposure factors*

Method	kVp	mA	sec	cm	
	Exposure factor				
Skull					
Frontal view	95	100	2.0	80	kxo-15
Lateral view	90	100	1.5	80	kxo-15
Temporal bone					
Axiolateral (Schuller)	90	150	1.5	60	kxo-15
Posterior profile (Stenvers)	85	200	0.4	60	kxo-15
Semi axial (Mayer)	90	200	0.4	60	kx 15
Paranasal sinus					
Postero anterior (occipito-frontal)	90	100	2.0	80	k 15
Postero-anterior (occipito-nasal)	95	100	2.5	80	k o-15
Oblique (Rhese)	90	100	2.0	80	kxo-15
Larynx					
Frontal view	65	100	1.5	100	kxo-8
Lateral view	60	100	0.75	100	kxo-8

METHODS AND APPARATUS

Toshiba xeroradiography equipment type XRA 101 2 has been used throughout the study The schema of xeroradiography is shown in Fig 1 and e plained according to the rder of procedure

1 *Selenium plate charging (sensitization)* The selenium coated metal plate is positively charged by corona discharge for sensitization. The charged elenium plate is used as a photo-sensitive plate instead of the usual film

The potential on the surface of the plate after charging will decay with the lapse of time even without radiation or light (dark decay) Therefore the pl te hould usually be charged just before the roentgen-ray exposure is made

2 *Roentgen xpo ure* The roentgen exposure is performed by the con entional roentgenographic apparatus. The X ray apparatus of Toshiba KXO-15 and KXO-8 were used in the present study

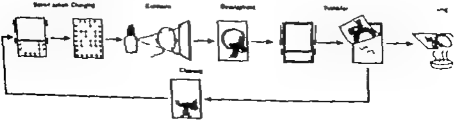

Fig. 1 Schema of xeroradiographical processing

XERORADIOGRAPHY AND ITS CLINICAL APPLICATION TO OTO-LARYNGOLOGY

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Xeroradiography, a kind of electrostatic and dry photographic method for radiography, has the advantages of higher definition and wider latitude than ordinary roentgenography. The authors have developed the xeroradiographic technique for clinical use and explored the diagnostic application of this technique to problems in the field of oto-laryngology.

The limitations imposed by the delayed recovery of the selenium plate during repeated uses were almost eliminated by using a special recovery promoting instrument. Various regions of interest to the oto-laryngologist such as the temporal bone, the paranasal sinuses and the larynx were studied.

INTRODUCTION

Xeroradiography is a new type of roentgenographic method (McMaster 1951, 1961; Nyerberg, Clark & Dessauer 1955; Taylor & Tenny 1955; Roach & Hilleboe 1955 a, b; Oliphant, 1956; Yoshimura, Sudo & Sakata 1960; McGonnagle 1961). It is a kind of electrostatic and dry photographic method. That is, by using a selenium coated and positively charged metal plate (photosensitive selenium plate) instead of the usual film, it eliminates the need for a liquid developer and fixer for roentgenography. Furthermore, the roentgenogram obtained by this method has wider latitude and higher definition.

There are many reports of xeroradiography in the fields of industrial examination, but only a few in the fields of medical examination. These are limited to the bone extremities (Hills, Stanford & Moore 1955), disease of the bone and joint (Campbell & Roach 1959), dental application (Pogorzelska-Stronczak 1963), diagnosis of breast tumor (Gould *et al.*, 1960), mammography (Ruzicka *et al.* 1965) and megavoltage treatment planning (Farmer, Fowler & Haggith, 1963).

In this paper, diagnostic applications of xeroradiography to oto-laryngology will be presented. Various regions of interest to the oto-laryngologist, such as the temporal bone, paranasal sinuses and larynx were studied.

the areas with higher charge attracting more powder than those with lesser charge

4 *Transfer* Although this powder image may be viewed readily with a viewing unit providing scattered illumination of the plate, ordinarily it is transferred to a plastic-coated paper by corona discharge

5 *Fixing* Then the transferred image is easily fixed by the vapor of an organic solvent (Trichlene) The vapor will soften the plastic coating of the paper sufficiently to fix the image of the powder on it. The fixed images appear to be as permanent as printer s ink

6. *Cleaning* The selenium plate can be re-utilized by applying a plate cleaning instrument (brush cleaner) Furthermore it is necessary to utilize a plate recovering instrument (relaxation unit) before repeated use With careful handling and cleaning the xeroradiographic plate may last for about a thousand successive exposures.

RESULTS

1 *Temporal bone*

The xeroradiogram of the temporal bone in axio-lateral projection in the Schüller position had good visualization The sharp outlines of the thin wall of the mastoid cells and the lateral sinus were clearer than an ordinary roentgenogram (Fig 4)

It was relatively difficult to obtain the petrosus region in posterior profile in the Stenvers position The apex and the upper and lower borders of the pyramid and the internal acoustic canal were well demonstrated by the present technique but the labyrinthal area was poorly demonstrated (Fig 5)

H wever the xeroradiogram of the tympanic cavity of semiaxial Projection in the Mayer position had fair visualization of the auditory ossicles (Fig 6)

2 *Paranasal sinuses*

It wa relatively difficult to obtain the xeroradiogram of the nasal cavities nd paranasal sinuses of a postero-anterior projection, but it was relatively easy t obtain an blique projection.

The frontal view of the skull had fairly good visualization. The nasal ca ity the nasal septum, the maxillary sinuses, the ethmoid cells, the orbital margin and the zygomatic arch were well demonstrated (Fig 7) The oblique view f the skull in the Rhese position had good visualization a well. The frontal and sphenoidal sinuses, the ethmoidal cells, and the profil view f the optic foramen were clearly demonstrated (Fig 8)

3 *Larynx*

It was rel tively difficult to obtain a xeroradiogram of the larynx and pharynx from frontal views, but very easy to obtain those from lateral views.

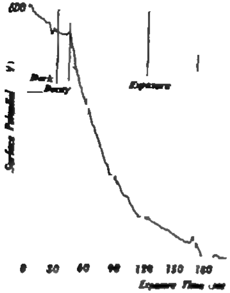

FIG. 2. Decay of surface potential (Dark decay and expo ure decay)

As indicated in Table 1 the suitable exposure factors varied with the object and methods

The charge on the plate surface will decay roughly in proportion to the radiation dose (Fig 2) But the decay characteristics seem to depend on roentgen tube voltage even if the dose rate is identical (Fig 3) Thus, after exposure the charge pattern remaining on the plate surface forms an electrostatic latent image.

3 *Developing* The electrostatic latent (invisible) image on the selenium surface may be revealed by spraying on the plate finely divided pigmented powder (Tonner) which has been given an electrostatic charge of the opposite sign by frictional electricity The powder will adhere to the plate

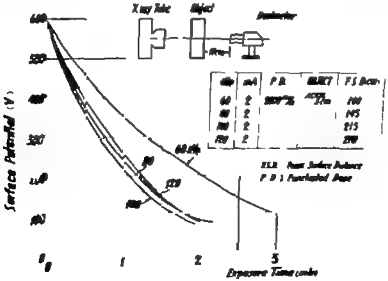

FIG 3 Decay characteristics depend on various roentgen-tube voltages

Fig. 8 Rhese view of the left, normal femal of 18 years of age

routine xerora liogram (Fig 12) but in many cases the aid of a contrast medium would be required as a rule (Kimura, 1960)

DISCUSSION

(1) Xeroradiography is a technique still in the early stage of its development f r medical aj plication, however it has certain advantageous charac teri ties a follows.

A higher image definition may be achieved because the resolving power of the xerograj hic plate i greater than that of the conventional roent genographic film (Roach & Hilleboe 1955 b Gould et al 1960) The out line of th im ges of xeroradiograpl s are particularly pronounced at the edge (edge-effect) because the trength f the field is considerably greater at the edge of a charged rea than it i at the center (Roach & Hilleboe 195 a) The wider latitude f xeroradiography makes the visualization of soft tissue with bon r air feasible

Furtherm re on may take into account rapid and dry processing as an ad ntage f xeroradiography

(2) A regard th relati n between exposure range and image contrast it wa bserved that exces ive exposure resulted in a dark image with l w contra t A imil r result ha been reported previously (Yoshimura, Sud & Sakata 1960) It has been lescribed that xeroradiographs of the hea l t k n at high kilo-v lt ges (120 to 140 kV) were of superior quality (Larm r Fowler & Haggith 1963) wherea under the conditions of our observation it wa somewhat different as indicated in Table 1 from their lescription

Care mu t be taken with the irradiation dosage because xeroradiography

Fig 4 Schüller view of the temporal bone normal female of 16 years of age
Fig. 5 Stenvers view of the petrous region, normal male of 31 years of age
Fig. 6 Meyer's view of the tympanic cavities, normal female of 20 years of age The auditory ossicles (maleus and incus) are fairly demonstrated
Fig. 7 Postero-anterior view of the paranasal sinus, normal male of 20 years of age

The lateral view of the larynx had the advantage of showing details of the soft tissue bone detail air passage and skin outline all within the same roentgen ray exposure range (Fig 9)

The images of an epipharynx-cancer were clearly demonstrated The outline of the posterior wall of the pharynx was pronounced because of the edge-effect of xeroradiography (Fig 10)

In the case of a malignant struma, the tumor was observed as a soft tissue shadow in xeroradiogram (Fig 11)

In some cases the shadow of the neck-cancer was demonstrated in the

cutting phenomenon due to air ionization (Wyerberg, Clark & Dessauer 1955) was very rarely observed as far as our experiments were concerned.

(3) The development of the image is one of the most critical steps in the process of producing images xerographically.

We have utilized the smoke method (Nagami *et al.* 1963) which is a mixed type of Cascade and Open chamber method (Hughes, 1959). It was observed that the smoke method could bring about excellent results.

(4) It is thought that moisture proofing is one of the most important factors to obtain good visualization of xeroradiographic images as well. One cannot obtain a good xeroradiogram under conditions of a high percentage of humidity. For this reason, the entire xeroradiographic process was performed in a moisture-controlled room.

(5) The limitations imposed by the problem of recovering the selenium plate before repeated use was almost eliminated by using a special recovery instrument which has an automatic thermostatic control. After the selenium plate is cleaned, the back of the plate is exposed to infra-red heating lamps for a short time at a temperature of 50 C, and then is rapidly cooled to room temperature by a blast of forced air (Ogawa, 1965).

(6) It was relatively difficult to obtain the xeroradiogram of a frontal view both of the skull and of the larynx, whereas it was very easy to obtain that of a lateral view.

The visualization of the object may have some relation to its size. The apparatus and structures which have a certain size such as the tympanic cavity, the mastoid cells, the nasal cavity, the paranasal sinuses, the pharynx and the larynx had good visualization.

But the apparatus which lie in the deep parts of the head and which have a finer size such as semicircular canals had poor visualization. It seems that a causative factor for it may be the insufficiency of image contrast or the inadequacy of roentgen ray quality. Further studies on these problems would be required.

As a whole, xeroradiography has a wider latitude which makes possible a roentgenographic examination of bone and tissue at the same time. The xeroradiographic image has a higher definition, moreover, the outlines of the images are particularly pronounced at the edge.

ACKNOWLEDGMENT

We wish to express our hearty thanks to Prof. Y. Miyoshi for his advice and guidance and to Mr. K. Oru in the Dept. and Mr. I. Ogawa in the Medical Electronic Dept., Tokyo Shibaura Electric Co. Ltd., for their technical help.

ZUSAMMENFASSUNG

Die Xeroradiographie ist ein neuartiges röntgenographisches Untersuchungsverfahren. Da statt des üblichen Filmes eine mit Selen überzogene geladene

FIG. 9 Lateral view f the l ryng. n m l mal of 60 rs f ag
FIG. 10 Lateral view of th ph rynx, f m l f 25 y rs of ge Th piphary nx tumor is clearly demon trated
FIG. 11 Later l vi w of a malign nt thyroi l tu to f m l f 51 rs f g
FIG. 12 Lateral iew f the larynx, n al f 50 y ars f g The neck ncer i l rl demonstrated

requires an increased exposure It has been reported that with higher kilo-voltage and filtration the patient will be greatly protected from radiation damage (Henny 1958)

The irradiation dose for xeroradiography of the skull according to our method is less than that of tomography of the same region The under

EFFECTS OF CHEMICAL ALTERATION IN THE ENDOLYMPH ON THE COCHLEAR POTENTIALS

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The scala media of the guinea pig cochlea was perfused with isotonic KCl, Ringer' solution and perilymph. The cochlea potentials were recorded during and subsequent t the perfusion. Our results indicated that in those animals perfused with perilymph the cochlear potentials were more remarkably depressed than in those perfused with KCl solu tion. We propose that high potassium concentration in the endolymph is indispensable for maintaining cochlear function while low potassium or high sodium media cause irreversible functional damage to th cochlea

The chemical determination of the concentration of monovalent ions in the cochlear fluid of the guinea pig by Smith, Lowry & Wu (1954) indicates that the endolymph contains high potassium (144 meq/L) low sodium (15.8 meq/L) and high chloride (107 meq/L) concentrations, while the perilymph has almost the same ionic composition as spinal fluid. The existence of this high potassium concentration in the endolymph was confirmed in different species by other investigators in the cat by Citron, Exley & Hallpike (1956) and in the turtle the frog and the lizard by Johnst ne Smith & Johnstone (1963) It is still unclear whether the ex istence of high potassium and low sodium concentration in the endolymph i essential for maintaining the high sensitivity of the hair cells of the organ of Corti. Recently Tasaki (1960) proposed that this peculiar ionic composition f the endolymph contributes to lowering the activity threshold f the hair cells of the org n of Corti

In order t study adequately the effect of potassium concentration in th endolymph upon cochlear potentials, we undertook to develop micro-techniques by which the endolymph could be replaced with a solution of known pota ium nd/or sodium ion concentration at a constant rate of perfusi n

Evidence will be presented which indicates that high potassium con entration in the endolymph is indispensable for maintaining cochlear function, while l w pot s ium or high sodium media cause irreversible functional d mage to the cochlea.

Thi research w supported i large part by grant NB 03016 from the National Institut of Health.

Metallplatte verwendet wird ist kein flüssiges Entwickeln und Fixieren nötig. Aus diesem Grunde wird die Methode Xero genannt. Wir erprobten die klinisch diagnostische Anwendung der Xeroradiographie in der Otolaryngologie. Die Begrenzung des Verfahrens, die dadurch entsteht dass der Selenüberzug erneuert werden muss, konnte durch Verwendung eines geeigneten Apparates fast beseitigt werden. Es wurden verschiedene Organe der Otolaryngologie untersucht so das Schläfenbein die Nasennebenhöhlen und der Larynx.

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The perfusates used in these experiments were mammalian Ringer's solution, isotonic KCl solution and perilymph. The sample of perilymph was taken from the contralateral cochlea. The round window was exposed in the left ear by the retroauricular approach. A glass pipette with a tip diameter of approximately 100 microns was mounted on a micromanipulator and slowly advanced into the scala tympani through the round window membrane. The perilymph was collected in this pipette by capillary action. The testing fluids were kept at room temperature (approximately 20 C)

C. Testing Procedure

Upon completion of the surgery the guinea pig was given 0.1 cc of D-tubocurarine chloride intravenously and placed on an artificial respirator. The head was tightly mounted on a specially designed metal holder and sound stimuli were delivered to the ear through a polyethylene tube. After CM, SP and AP elicited by the tone burst were recorded, the scala vestibuli was widely opened in the fourth turn so as to visualize Reissner's membrane. At times a droplet of methylene blue solution was introduced into this window in order to facilitate the visualization of Reissner's membrane. Then Reissner's membrane was widely torn with a small glass hook. Upon completion of the rupture of Reissner's membrane the glass pipette electrode was inserted into the scala media through the spiral ligament to measure EP. Finally the perfusion pipette was advanced to the scala media in the basal turn until a positive EP was registered on the electrometer. During the preliminary period before the initiation of the perfusion, CM, SP and AP were recorded immediately after each of these steps.

The perfusion was then carried out by applying positive air pressure to the perfusion pipette. The rate of the perfusion was controlled by adjustment of this positive pressure. Usually 20 to 40 minutes were required to inject 1 to 2 microliters of the perfusate. Sometimes the tip of the perfusion pipette would become blocked, and the perfusate could not be introduced smoothly into the scala media. To make certain that the perfusion was being effectively done it was necessary to note whether the meniscus at the oil-perfusate interface was moving at a constant rate and this was done under high magnification of an operating microscope. The cochlear potentials were measured at 15 second intervals until they became stabilized, at which time records were taken every 30 seconds for approximately one hour after initiation of the perfusion.

Upon completion of the perfusion, the pipette was removed from the cochlea and examined with the calibrated ocular micrometer in order to calculate the volume of the fluid injected.

In almost every experiment, the dc resting potential of the organ of Corti was measured after completion of the experiment. A glass pipette electrode with a tip diameter of approximately 1 micron was introduced

METHODS

A Arrangements for Recording Potentials

The experiments were carried out on guinea pigs anesthetized with pentobarbital sodium 40 mg/kg body weight intraperitoneally The trachea of the animal was intubated and the left jugular vein was cannulated for intravenous injection The right cochlea was exposed by the classical ventrolateral approach In order to measure the endocochlear potential (EP) a small fenestra was made over the spiral ligament of the basal or the second turn so that a glass pipette electrode mounted on a micromanipulator could be inserted into the scala media The pipette electrode with a tip diameter of 3 to 5 microns was filled with isotonic KCl solution in which a chloride-coated silver wire was immersed When recording the cochlear microphonics (CM) summating potential (SP) and action potential of the auditory nerve (AP) the differential electrode technique (Tasaki & Fernández, 1952) was employed These electrodes were placed in the basal turn and in some cases a second pair was inserted in the second turn Differential electrodes were placed symmetrically with the glass pipette electrode positioned between them so that all three were aligned in the same axis. A chloride-coated silver wire placed on the neck muscles served as the reference electrode EP was measured by means of an electrometer and CM SP and AP were displayed on an oscilloscope and photographed Sound stimuli used were tone bursts of 4000 cps at approximately 75 dB (re 0 0002 dynes/cm^2) The individual stimuli lasted 8 msec with fast rising and falling time

B Perfusion of Scala Media

The surgery preparatory to perfusing the scala media consisted of first making a second fenestra over the spiral ligament of the basal turn and then rupturing Reissner's membrane at the fourth turn so that a glass micropipette filled with the perfusate could be inserted into the scala media and the cochlear endolymph could be replaced with the perfusate without noticeable increase of the cochlear pressure This fenestra was made close to the oval window in order to insure that the perfusate reached the area in which electrodes were placed The perfusion micropipette with a tip diameter of approximately 10 to 30 microns was connected through a polyethylene tube to a source of compressed air the pressure of which could be adjusted by a stopcock This perfusion pipette also served as a microelectrode for measurement of EP the dual function being accomplished by inserting a chloride-coated silver wire into the perfusate in the pipette The rest of the lumen of the pipette was filled with air free paraffin oil The meniscus at the paraffin oil perfusate interface could be easily visualized and its excursion measured with a calibrated ocular micrometer to determine the amount of perfusate injected into the scala media

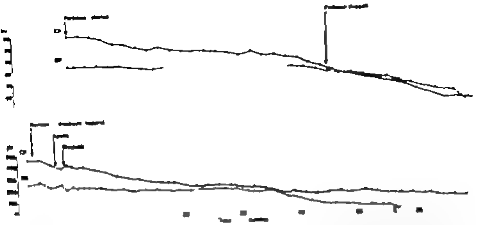

FIG. 1 An example of cha ges in EP nd CM during and after perfusion f the scala media with 2.18 microliters f isotonic KCl solution. *EP* and *EP* represent the endocochlear potential in the basal and second turn respectively Similarly *CM* and *CM* indicat cochlea microphonics in the basal and second turn. Perfusion is started with 9 ml . Sound stimulus 4000 cps tone burst at pproximately 75 dB.

other hand, a 50 per cent drop in CM was observed 30 to 60 minutes after the perfusion. AP was depressed more slowly than was CM but the overall pattern was similar for both. SP changed in different ways during this period. In most cases the negative SP gradually decreased in magnitude but in a few SP reversed its polarity Fig 1 shows the behavior of EP and CM during and after the perfusion of the scala media with isotonic KCl solution.

When perilymph was used as the perfusate, its effect on the cochlear potentials was striking. In fact, EP was maintained at or above its original v lue during the perfusion, but CM began to decline progressively On the average CM dropped to 50 per cent of the original magnitude within 10 minutes after initiation of the perfusion and then the rate of its reduc ti n became slow until it reached the post mortem level. EP was also progres ively depressed after perfusion with perilymph. Most of the cases h wed a 50 per cent drop of EP 20 to 30 minutes after the perfusion. AP decreased to 40 per cent of its initial magnitude within 5 minutes. Unlike CM and AP SP usually increased in it negativity during the initial period of the perfusion This temporary increase was followed by a gradual decrease after a certain tim lapse The pattern of the change in SP ried considerably among individuals. In several animals, SP did not exhibit orderly changes and it might increase decrease and again increase wherea amplitudes of both CM and AP decreased in an orderly progression Fig 2 hows n example of changes in CM and EP during and subsequent to perfusion of the scala media with perilymph.

When Ringer solution w s used as the perfusate, changes in the ochlear potential were imilar to those observed in perfusion of the scala

into the organ of Corti through the round window membrane In each animal three separate measurements were taken, the electrode being withdrawn and reinserted each time and an average value obtained

In a few animals the temporal bones were perfused intravitally with Heidenhain's Susa fixature and saved for further histological study In cases where the temporal bones were not preserved, methylene blue was injected into the scala media in order to detect possible damage to the cochlear partition caused by excessive hydrostatic pressure during perfusion

RESULTS

As a control experiment we examined the effect of rupture of Reissner's membrane in the fourth turn upon the cochlear potential in the basal and second turns In the basal and second turns magnitudes of EP and CM elicited by 4000 cps tone bursts were measured before and after the rupture of Reissner's membrane and were found to remain essentially unaltered for one to two hours, providing excess fluid was removed from the auditory bulla

Thirteen guinea pigs were used for the perfusion of the scala media with isotonic KCl solution six for perfusion with mammalian Ringer's solution and eighteen for perfusion with perilymph The quantity of the perfusate varied in each experiment ranging from 0.24 to 2 24 microliters The rate of the perfusion also varied from a maximum of 0 075 to a minimum of 0 014 microliters per minute with most cases falling in the range of 0 020 to 0 030 microliters per minute When the rate of the perfusion was constant and slow enough to avoid hydrostatic damage EP in the basal turn began to rise slowly 1 minute after initiation of the perfusion This rise in EP was usually less than 10 mV then reached a plateau and gradually returned to the original value This initial increase of EP was recorded in almost all cases and its change was not related to the perfusate used but rather to the rate of the perfusion This temporary increase of EP was usually associated with an increase of the negativity of SP regardless of its sign prior to perfusion On the other hand there were only slight changes in the magnitude of CM and AP during this initial period as long as care was taken to remove any excess fluid from the bulla

When 3 to 4 minutes had elapsed all responses except EP started to decline gradually The rate of their depression was not proportional to the time course and the degree of their depression differed for each of the cochlear potentials

When the endolymph was replaced with isotonic KCl solution CM in the basal turn was generally found to be reduced to 80 to 90 per cent of the original magnitude 10 minutes after the perfusion while EP was well maintained at a high level EP dropped to 70 to 80 per cent of its original value 50 to 60 minutes after initiation of the perfusion on the

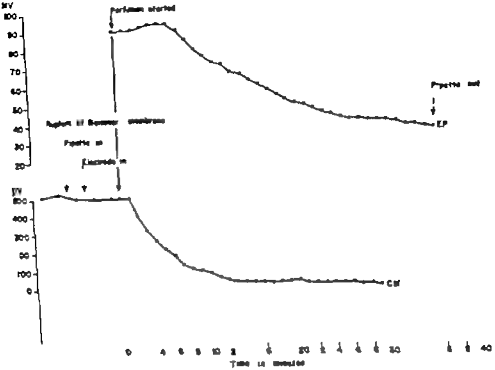

FIG. 2. Changes in EP and CM during and after perfusion of the scala media with 1.34 microliters of Ringer solution. EP and CM are measured in the basal turn. Sound stimulus: 4000 cps tone burst at approximately 60 dB.

As long as the periodic measurements for the cochlear potentials were continued, up to 30 minutes, or longer after the perfusion was stopped, none of the experimental animals showed any tendency to recover. The cochlear potentials did not exhibit any sign of the recovery process in either the basal or second turns, even when isotonic KCl solution was used as the perfusate. In some cases, the perfusate was replaced later with artificial endolymph containing one part of isotonic KCl solution and three parts of Ringer's solution. Cochlear potentials in the basal turn did not show recovery at all but continued to decline.

The negative dc potential within the organ of Corti was tested when changes of the cochlear potential leveled off. Relatively large variations in the negative value were found. The average values obtained were 75 mV in KCl-treated animals, 44 mV in perilymph-treated, and 48 mV in Ringer treated. The average values appeared to indicate a slight reduction but no significant correlation was found between the magnitude of the negative potential found in the organ of Corti and the degree of depression of CM.

DISCUSSION

The fact that the destruction of Reissner's membrane in the fourth turn resulted in no appreciable changes in the cochlear potentials in the

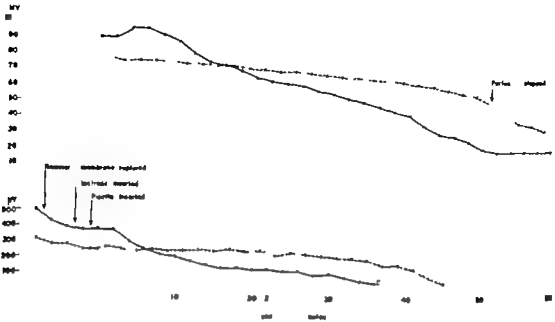

FIG. 2. Changes in EP and CM during and subsequent to perfusion of the scala media with 1 40 microliters of perilymph Perfusion is started with 0 minute

media with perilymph and no significant differences were found between the two groups although the number of cases was small Fig 3 shows the changes in CM and EP during and after perfusion of the scala media with Ringer s solution

The histogram shown in Fig 4 indicates distribution of the response decline of EP and CM after perfusion with KCl solution and perilymph It can be seen that there is a wide variation within each group However it does appear that in those animals perfused with KCl solution the distribution is not as wide as in those perfused with perilymph even though the rate and volume of injection varied from one animal to another Looking at the histogram it seems that the rate and volume of perfusion are more critical when perilymph is used

Simultaneous recording of the cochlear potentials in the basal and second turns was carried out in 17 cases The quantity of the perfusate varied in each experiment ranging from 0 3 microliters to 2 3 microliters The depression of all the cochlear volume critical potentials was generally related to the amount of the perfusate A small volume of perfusate produced depression of the cochlear potentials in the basal turn and in order to produce a comparable depression in the second turn it was necessary to introduce a much larger volume of perfusate In other words more than 1 microliter of the perfusate caused a parallel reduction of CM and EP in both basal and second turns with a certain time delay in the second turn as shown in Figs 1 and 2 on the other hand a relatively small quantity of the perfusate depressed CM and EP more remarkably in the basal turn than in the second turn

Fig. 3 Cha ges i EP and CM during nd fter perf sion of the scal media with 1.24 microliters of Ri ger's solution EP nd CM are measured in the basal t rn. Sound stimulus 4000 cps tone burst t pproximat ly 80 dB.

A long as the periodic measurements for the cochlear potentials were continued up to 30 minutes, or longer after the perfusion was stopped, none f the experimental animals showed any tendency to recover The cochlear potentials did not exhibit any sign of the reco ery process in either the basal or second turns, even when isotonic KCl solution was used as the perfusate In some cases, the perfusate was replaced later with artifici l end lymph containing one part of isotonic KCl solution and three part of Ringer s solution. Cochlear potentials in the basal turn did not how recovery t all but continued to decline

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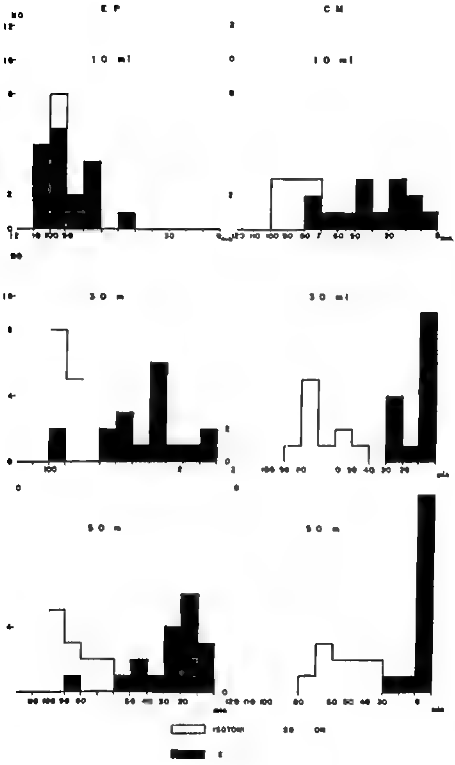

Fig. 4. Histograms showing response decline of EP and CM in the basal turn after perfusion of the scala media with isotonic KCl solution and perilymph. The ordinates indicate the number of animals and the abscissae the responses expressed in per cent of the initial value. The white bars indicate the perfusion with isotonic KCl solution and the solid black ones the perfusion with perilymph. Time is shown in minutes after the beginning of the perfusion.

lower turns, including EP indicates that both EP and the cochlear responses recorded by the electrodes in the basal and second turns as described are generated within the basal turn and that the removal of Reissner s mem brane in the fourth has little effect on the electrical or acoustical property of the basal and second turns.

Tasaki Davis & Eldredge (1954) tested the effect of hydrostatic pressure within the scala media on the dc potential in the scala media. Increase of the pressure in the scala media caused an increase in the dc potential and negative pressure applied to the scala media resulted in reduction in the dc potential. They concluded from their experiment that the slow modula tion of the dc potential is caused by some structure that lies on the basilar membrane Later Davis (1957) postulated that the downward movement of the basilar membrane caused hyperpolarization of the hair cells of the organ of Corti, and consequently the dc potential in the scala media is increased by this change The appearance of the initial increase in EP after perfusion can be explained as the direct effect of pressure increase in the scala media by the perfusion. The slow recoveries may represent gradual equalization of pressure by slow movement of the cochlear fluid. O the basi of our experimental data, there is little doubt that the magnitude f this temporary increase in EP is not dependent upon the medi injected into the scala media but upon the rate of the perfusion

Changes in the cochlear potentials produced by replacement of the cochlear end lymph with perilymph or Ringer's solution are clearly dif ferent from those produced by perfusion of the scala media with isotonic KCl lution It i apparent that EP is depressed more by replacement of the endolymph with potassium poor perfusate than by potassium rich medium H wever there is no abrupt drop in EP but, instead a gradual decline It i g nerally accepted that EP is maintained by the metabolic activity f the stria v scularis (Tasaki & Spyropoulos, 1959)

The fact that any alteration of the chemical composition of the endo-lymph resulted in the gradual decline of EP indicates that potassium rich endolymph is essential t n rmal function of the stria vascularis

In contrast to the changes in EP CM and AP decline abruptly after the perfusion of the scala media with perilymph or Ringer s solution Da i *et al* (1953) demonstrated that if Ringer's solution wa injected int th scala media, there was a rather rapid failure of all electrical responses. In our experiment, complete replacement of the end lymph in the basal turn was tt mpted and the depression of CM was found to be more closely dependent n lowering of the potassium concentration in the ndolymph than w s EP What comprises this event is conjectural at present Davi (19 7) postulated that a high potassium concentration in endolymph might be essential to preserving the colloidal state of the tectorial membrane T saki (1960) found that the squid axon membrane and th toad nodal membrane treated with potassium rich media and sub-jected t nodal polarization, were extremely sensitive to changes in hydro-

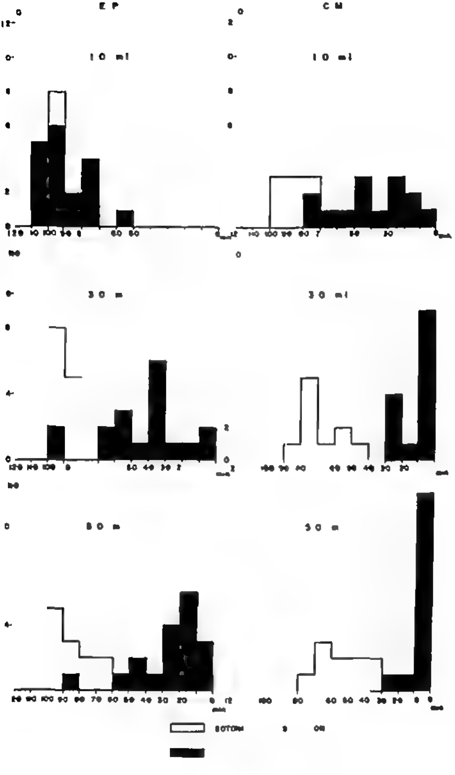

Fig 4 Hi togr m how g respo decll e f EP a d CM i th ha l turn fter per f si n of tl scal med with isot ni KCl soluti n a d peril mpl The rdi l indicates th number f nimal nd the absci sa th response pressed in per ce t f the i itial l e Th whit bars i di t tl perf i with isot nic KCl luti n and the solid black es th perfusi n with perilymph. Tim i hown i mi utes after the beginning f the perfu i

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ratio of potassium to sodium has been demonstrated in endolymph of *elasmobranchs* as well as in *teleosts* (Enger 1964). This seems to indicate that phylogenetically this feature devel ps quite early whereas the high EP is m re characteristic of higher animals such as reptiles and birds (Smith & Fernández, 1962). The higher ratio of potassium to sodium in the endolymph seems to be related to the develoj ment of hearing. Our results show that in guinea pigs potassium rich endolymph is necessary not only t normal metabolism of the stria vascularis but also to maintain high sensitivity of the hair cells of the organ of Corti to sound and low potassium or high sodium media in the scala media cause irreversible lepression of the cochlear potentials. It is reasonable to a sume that our experimental data obtained in guinea pigs is applicable to cochleas of other mammals. Such data may ffer a clue to the origin of certain types of sensori neural deafness. More inf rmation is needed concerning the process responsible for this irreversible damage to the cochlear function and may contribute to better understanding of the nature of sensori-neural deafness.

CONCLUSION

Th ffect of perfusion of the scala media with perilymph isotonic KCl and mammalian Ri ger' solution w tested i normal guinea pigs.

1. The rupt re f Rei sner' membra in th fourth turn did not ignificantly modif the cochlear potential in the basal or th second turn.

2. Th temporary increase of EJ associ ted with a increase f the egati ity of SP shortly after perfusion was produced by an increase f the hydrostatic pressure within the scala media whi h caused downward di placement of the basilar membran

3. When the end lymph w replaced will isotonic KCl solution CM was generally found t be reduced t 80 t 90 per cent of the iginal magnitude 10 minutes fter the perfusion, and a 50 per cent drop of CM wa observed 30 t 60 minutes fter the perfusion. CJ on the ther h d, reached it 80 to 90 per cent value 50 t 60 min tes ft r th i itiation of the perf ion.

4. Although there was a wid variation, when perilymph was used a th perfusat CM generally began to decl progres iv ly dropped t 50 per cent f its original value within 10 minutes fter the perfusion and then reached the post mortem lev l. EP showed a 30 pe cent drop 20 to 30 minutes fter the perfusi n.

5. The effect f Ringer' solution as the perfusate was similar to that observed in th perfusion of the scala media with perilymph and no significa t differences were found between the tw groups.

6. Non f the cochlear potentials showed ny tendency to recover after the perf sion of the scala media with these perfusates.

7. The negative d potential within the orga f Corti appeared to show a sl ght reduction fter the perfusion of the scala media, but n significant correla tion was found between the magnitud of the n gative potential in the organ of Corti and the d gree f depression of CM

8. W cann t dismis the possibility of th mechanical destruction of the

static pressure and to mechanical distortion of the membrane These results led him to a reasonable explanation concerning the mechanism whereby mechanical energy is transformed into electrical energy at the hair bearing end of the hair cells and he ascribed the high sensitivity of this transducer action to the existence of EP and high potassium concentration in the endolymph It can be reasonably assumed that perilymph or Ringer s solution injected into the scala media did not affect cell bodies of the hair cells of the organ of Corti because these are isolated from the fluid in the scala media by the reticular layer This idea is also confirmed by the fact that the negative dc potential in the organ of Corti was not abolished but slightly reduced by the replacement of the endolymph with perilymph As the dc potential in the organ of Corti was measured by a fine micropipette it is certainly the intracellular potential and represents the activity of the hair cells Presumably the alteration of the chemical composition of the endolymph might result in reduction of the sensitivity of hair cells to mechanical stimulation This can explain the fact that the hair cells in the vestibular apparatus maintain their high sensitivity without a high dc potential in the endolymphatic duct

Another prominent feature observed after perfusion of the scala media with either isotonic KCl Ringer s solution or perilymph is the irreversible and progressive depression exhibited by all cochlear potentials Very probably it is that changes in the chemical composition of the endolymph cause permanent dysfunction of the cochlea

Mechanical destruction of the cochlear partitions particularly the organ of Corti, caused by the perfusion of the scala media is always a possibility and it is very difficult to decide how much influence it exerts on the changes of the cochlear potentials To substantiate this possibility one would insist that the changes of the cochlear potential observed in our experiments are always irreversible We cannot dismiss this explanation of our data Nonetheless it does not adequately account for the different effects of the various perfusates on the cochlear potentials, even though it is true that perfusion rate varied considerably between individuals In addition to this, the various perfusates were introduced directly into the scala media of the basal turn yet their effect on the cochlear potentials in the second turn is similar to that in the basal turn From these facts, we can assume that the mechanical damage to the cochlear partition caused by the perfusion is minimal and that the observed changes of the cochlear potentials were due to alteration of the chemical composition of the endolymph

There are other possible ways to account for our data Oxygen tension and pH of the perfusates may modify the cochlear potential However there is not enough knowledge available concerning these biophysical characteristics of the endolymph and therefore it is impossible at present to evaluate the importance of these factors The ionic composition of the endolymph has been analyzed in various animals A comparatively high

VESICLES AND BASEMENT MEMBRANE CHANGES ASSOCIATED WITH HYDROPS OF THE SACCULE AND ENDOLYMPHATIC DUCT AND SAC

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Th significa ce f vesiculations of the m mbranous labyrinth are discussed from the point of iew of normal and i creased pi ocytosi activit Basement membran changes i the membranou w ll of the saccule are demonstrated in patient with hydrops of the saccule and endolymphatic duct and sac. Th esiculation and basement m mbran changes are believed t indicat the movement of large amounts of fluid across the membrane w lls.

Th temporal bones from a patient with marked distention of the saccule and end lymphatic duct and sac associated with "inherited sensori neural deafness have recently been studied in our laboratory The details of the pathological findings will be presented in a separate report. Very pronounced hydropic dist ntion of the saccule and endolymphatic duct and sac was present bil terally (Fig. 1) with normal caliber of the cochlear duct, utricle and semicircular canals Throughout the saccule, semicircular canals and e d lymphatic duct and sac numerous vesicles were present with protru i n into the lumina. Varied size vacuoles were observed within the cyt plasm of the epithelial cells of these structures (Fig 2) The vacuoles were either clear or contained faintly eosinophilic amorphous material In addition hyaline protrusions containing vesicles and round PAS positive tructures were observed in the saccule and endolymphatic d ct which in some areas were attached t the wall of these structures and in ther areas were lying free within the lumina (Figs 3 and 4) These were irregula in size and shape The wall of the saccule revealed several thicker areas containing pale eosinophilic o clear material in which rounded clumps of PAS positive material were discernible (Fig 5)

S pported in part by grants from USPHS NB-06606 and Deafness Research Foundation, New York, nd Hope for Hearing Research Foundation, U iversity f California, Los Angeles, Calif

organ of Corti caused by the perfusion of the scala media yet we can safely assume that the observed changes of the cochlear potentials were due to the alteration of the chemical composition in the endolymph because the changes in the cochlear potentials in the second turn followed these in the basal turn in similar course but with a certain delay time

9 Our results showed that high potassium concentration in the endolymph is indispensable for maintenance of the cochlear function while low potassium or high sodium media cause irreversible functional damage to the cochlea

ZUSAMMENFASSUNG

Die Scala media der Meerschweinchen Cochlea wurde mit isotonischem KCl Ringerscher Lösung und Perilymphe perfundiert Während und nach der Perfusion wurden die Cochlea Potentiale aufgezeichnet Nach unseren Resultaten sind die Cochlea Potentiale in Tieren die mit Perilymphe perfundiert wurden, stärker unterdrückt als in denen die mit KCl Lösung perfundiert wurden Zur Erklärung schlagen wir vor dass eine hohe Kaliumkonzentration in der Endolymphe unerlässlich für die Aufrechterhaltung der Cochlea Funktion ist während Lösungen arm an Kalium oder reich an Natrium irreversible Funktionsschädigungen der Cochlea hervorrufen

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Fig. 2. Vesicles in the epithelium of the horizontal semicircular canal with protrusion into the lumen. Hematoxylin and eosin, 250

with the creation of large clearly demarcated fluid spaces. These fluid spaces were separated from the perilymphatic space only by a basement membrane.

The term pinocytosis refers to the bulk uptake of fluid by cells. Fawcett (1965) describes with the electron microscope the various types of pinocytosis observed by absorbing cells, all of which result in a quantity of fluid appearing within the cell cytoplasm in the form of a vacuole. The vacuoles move slowly inward toward the cell center becoming progressively smaller. Fawcett emphasizes that these droplets are easily visible with the light microscope.

The vesiculations found in the membranous canal of normal temporal bones have been of the size and number to suggest their presence as part of the normal pinocytosis activity of the membranous epithelial lining cells. However when the size and number of these vesicles increase to the proportion described in various accounts of endolymphatic hydrops, it

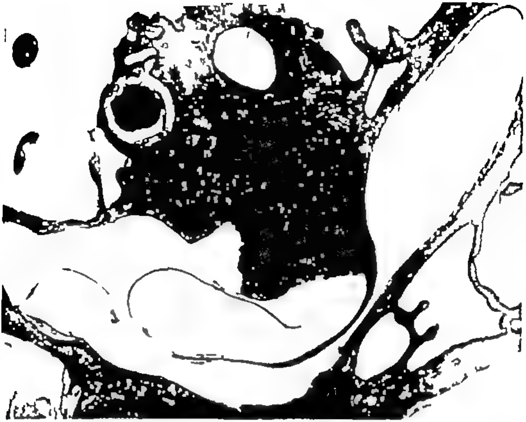

Fig. 1. Horizontal section showing hydropic distention of the saccule, saccular duct and endolymphatic duct and sac. Hematoxylin and eosin, ×8.

DISCUSSION

Vesiculations in the membranous labyrinth have been described by many authors. Hallpike & Cairns (1938) described excrescences of subepithelial fluid collections in the superior and lateral semicircular canals of two cases of Menière's syndrome. However, Hallpike observed similar vesicles in the semicircular canals of seven out of ten routinely examined temporal bones in patients between the ages of 40 and 60 years with no history of Menière's disease. Altmann & Fowler Jr. (1943) observed vesiculations in two of three cases of Menière's syndrome within the semicircular canals and in the utricle and saccule. Lempert *et al.* (1952) found vesiculated epithelial excrescences varying in size and number in the membranous semicircular canals of six consecutive patients with Menière's disease following partial labyrinthectomy. Berkmen (1966) examined 200 temporal bones from 100 patients selected at random and found vesiculations of the semicircular canals in all but one. Vesiculations have also been observed in our laboratory within the semicircular canals of temporal bones removed routinely at autopsy where no history of Menière's syndrome was present and where no abnormalities were found.

Utilizing the electron microscope, Smith (1956) has described branching within the cytoplasm of the epithelial cells lining the body of the utricle

Fig. 4 Endolymphatic duct showing irregular hyaline protrusions PAS. 100.

in the wall of the saccule in an area of early vesiculation In Fig 3 we see another area in the wall of the saccule again demonstrating with PAS reactio the presence of the rounded PAS positive hyaline structures within vesicle excrescences A rim of flat epithelial cells still contains the material. The PAS positive structures here again suggest derivation from the basement membrane of the saccule wall

It is believed that the vesiculations and basement membrane changes described are indicativ of the movement of large amounts of fluid across the m mbrane walls.

ACKNOWLEDGMENTS

The author is indebted to D Victor Goodhill for his encouragement and guidance d t Mi Doris Donahue for her invaluable technical s istance.

ZUSAMMENFASSUNG

Die Bedeutung on calkulären Formationen des membranösen Labyrinths wird unter dem Gesichtspunkt von normaler und gesteigerter Pinocytosis-Tätig-

Fig 3 Saccul wall Note outpouching of porti n of wall int lumen Several round PAS positive tructures are present within thi protruded area PAS × 170

would seem logical to attribute this increase to the shifting or attempt to shift unusually large amounts of fluid across a membrane wall

Reidbord & Spitz (1966) performed a very interesting experiment whereby sea water and fresh water were perfused into the respiratory tract of rats and the ultrastructure of the lungs was examined The normal alveolar wall consists of a basement membrane separated from air on one surface by alveolar epithelial lining cells and is on the other side adjacent to the capillary endothelium This drowning of the rat lungs resulted in changes involving vacuolization of the lining epithelial cells as well as changes in the basement membrane They describe many circular and irregularly rounded structures within the capillary lumina, in the septal areas and within the alveolar spaces. These bodies occasionally impinged on surrounding structures With the electron microscope the authors demonstrated outpouchings of basement membrane material from the basement membrane and continuous with it by a narrow neck The authors felt that these changes represented the movement of large amounts of fluid Vacuoles were also seen in the basement membrane substance Reidbord & Spitz speculate that the defects in the usually completely covered basement membrane accounted for even further alterations in interchange of fluid across the alveolar wall

In our case break up of basement membrane material could be demonstrated in several areas by PAS reaction Fig 5 shows such an area

FIG. 4 Endolymphatic duct sho ing irregula hyaline protrusions. PAS, 190.

in the wall of the saccule in an area of early vesiculation In Fig 3 we see another area in the wall of the saccule again demonstrating with PAS reaction the presence of the rounded PAS positive hyaline structures within vesicle excrescences. A rim of flat epithelial cells still contains the material. The PAS positive structures here again suggest deri ation from the basement membrane of the saccule wall

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ZUSAMMENFASSUNG

Die Bedeutung vo ellkulären Formationen des membranösen Labyri ths wird unter dem Gesichtspunkt von normaler und gesteigerter Pinocytosis-Tätig-

FIG 5 Saccul wall d m nstrating thick ning by am rphous material and rounded clumping of basement membrane materi l PAS, 625

kelt erörtert Veränderungen der Basalmembran in der membranösen Wand des Sacculus werden bei einem Patienten mit Hydropsie des Sacculus und des endolymphatischen Ductus und Saccus gezeigt Man nimmt an dass die vesikulären Formationen und Veränderungen der Basalmembranen die Bewegung von grossen Mengen von Flüssigkeit durch die Membranwände anzeigen

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ELECTRON MICROSCOPIC STUDIES OF ADENOSINE TRIPHOSPHATASE ACTIVITY IN THE STRIA VASCULARIS AND SPIRAL LIGAMENT

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An enzyme for fluid transport, adenosine triphosphatase, has been studied in the stria vascularis and spiral ligament in the inner ear using various modifications of histochemical techniques for electron microscopy. We found enzyme activity appeared on the surfaces in the complex folds between the epithelial cells and on the surface facing the endolymph. Capillary basement membrane and mitochondria also showed marked activity. These findings are what one would expect of the stria vascularis considering its probable role in fluid transport and the findings of ATP-ase localization elsewhere.

INTRODUCTION

The stria vascularis and its underlying connective tissue have been regarded by most investigators as the source of endolymph. Many have studied its function by means of various histological and chemical techniques (Altmann & Waltner, 1947; Rüedi, 1951; Saxén, 1951; Mygind, 1952; Smith, 1957; Naftalin & Harrison, 1958; Engström, Sjöstrand & Spoendlin, 1953; Yamamoto & Nakai, 1964; Choo & Tabowitz, 1964, 1965).

Several enzymes have been localized by histochemical, light microscopic methods to various areas of the stria vascularis (Vosteen, 1961; Gerhardt, 1961; Schätzle & Musebeck, 1962; Spoendlin & Balogh, 1963; Koide, Yoshikawa & Morimoto, 1962). Because of the complex morphology of the stria vascularis, light microscopy must be augmented by electron microscopy for an accurate determination of the actual sites of enzyme activity.

Within recent years the combination of histochemical techniques with those of electron microscopy has resulted in successful demonstration of end products of several types of enzymatic activity, especially the phosphatases

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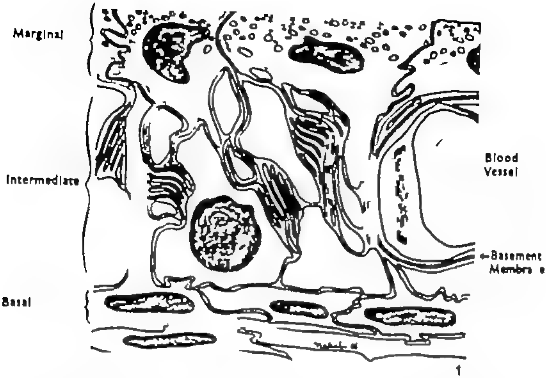

FIG. 1. Stria vascularis. Three types of cells, marginal (or dark), intermediate and basal (or light). The marginal cells face endolymph. Basal cells form the layer next to the spiral ligament and intermediate cells are found between. Complex folding and interdigitation of cell processes tremendously increase each cell's area. These surface membranes all show ATP-ase activity, suggesting that they have fluid transport capability.

at a fine structural level (Essner, Novikoff & Masek 1958; Molbert, Duspiva & Deimling 1960; Torack & Barrnett 1961; Wersäll, Hilding & Lundquist 1961; Hilding & Wersäll 1962; Schulze & Wollenberger 1962; Ashworth, Luibel & Stewart 1963; Sabatini, Bensch & Barrnett 1963; Marchesi, Sears & Barrnett 1964; Hilding 1965). Each investigation has been forced to arrive at a compromise between good preservation of fine structure and the risk of interference with the enzyme under consideration. Deliberate inhibition of a portion of enzyme activity is usually a prerequisite of finely detailed localization. The inner ear presents additional problems for enzyme studies because of its inaccessibility and fragility.

The present report is concerned with the histochemical localization of ATP-ase activity of the stria vascularis and spiral ligament. At the present time there is no standard technique for revealing the location of this enzyme for electron microscopy. Several different methods were used to study this enzyme.

Adenosine triphosphatase or ATP-ase is associated in other tissues with fluid transport. For instance Dunham & Glynn (1961) and Hayashi, Auditore & Uchida (1964) have dealt with the biochemical characteristics of Na

TABLE 1

				REACTION SITE				
				Stria vascularis			Spiral ligament	
Procedure	Prefixation	Wash with sucrose	Incubation medium	Endolymphatic surface	Folded membranes	Mitochondria	Cell membrane	Mitochondria
1	Osmic	2 hrs.	Wachstein-Meisel, 10 minutes	+	+	0	+	0
2	Formalin-sucrose	2 hrs.	Wachstein-Meisel, 10 minutes	+	+	0	+	+
3	Glutaraldehyde	2 hrs.	Wachstein-Meisel, 10 minutes	+	0	0	0	0
4	Glutaraldehyde and freezing	2 hrs.	Wachstein-Meisel, 10 minutes	+	+	0	+	+
5	None	None	Modified Wachstein-Meisel, 5 minutes	+	0	+	0	+
	None	None	Modified Wachstein-Meisel, 15 minutes	+	+	+	+	+
6	Controls, (see text for details)			0	0	0	0	0

and K transport and its relationship to ATP-ase. Several papers have appeared in regard to its electron microscopic localization. Toreck (1965) reported its relationship to brain capillaries. Marchesi, Sears & Barrnett (1964) discussed its localization in the eye. Because the stria vascularis supposedly secretes endolymph it is logical to suppose that it is rich in ATP-ase. Ilnum (1965) has confirmed this supposition in biochemical assays. The purpose of this paper is to present electron microscopic observations on the sites of ATP-ase activity in the stria vascularis and related connective tissue.

MATERIALS AND METHODS

The inner ear structures of anaesthetized guinea pigs were removed and immediately placed in an appropriate reagent. Much of the bone surrounding the cochlea was dissected away and Reissner's membrane was torn exposing the stria vascularis and spiral ligament to the chemicals.

In the preparation of tissue the following procedures were employed

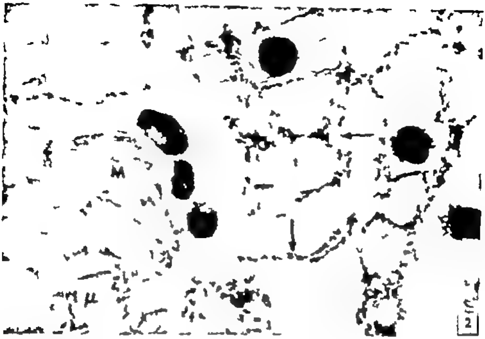

Fig. 2. Osmium fixed marginal cell following incubation with ATP as substrate. The reaction product (arrows) is present on the infolded plasma membrane but not on the mitochondria (*M*). Pigment granules (*P*) are present normally in this area. × 23 000.

(1) Tissue was fixed for 3 minutes in cold buffered osmium tetroxide 1%. After washing in cold 0.44 Mol sucrose the tissue was incubated according to the method of Wachstein & Meisel (1957) for adenosine triphosphatase containing lead nitrate as the capture reagent for 20 minutes in room temperature. Because the accumulated precipitate of lead phosphate is opaque in the electron beam, conversion to lead sulfide is unnecessary.

(2) The specimens were fixed in cold 10 per cent formalin with 4.0 per cent sucrose buffered to pH 7.2 for 1 hour. After this prefixation the tissue was washed in cold cacodylate buffer (pH 7.2) containing 0.44 Mol sucrose for 2 hours. Then the material was incubated in the standard Wachstein-Meisel medium at pH 7.2. Incubation was carried out at room temperature (20 C) for up to 10 minutes.

The same procedures were followed in other experiments in which ATP in the incubating medium was substituted for by β glycerophosphate or Adenosine 5 monophosphate at equimolar concentration.

(3) Tissues were fixed for 30 minutes in cold (4 C) 2% glutaraldehyde buffered to pH 7.2 with 0.05 Mol cacodylate. After this prefixation the same procedure as (2) was followed.

(4) Following prefixation with glutaraldehyde the specimens were frozen on a CO_2 cold stage to disrupt membrane barriers. Processing was then carried out as above.

(5) Without any prefixation the material was incubated in a mixture derived from Marchesi consisted of 80 mMol tris (hydroxy methyl) amino-

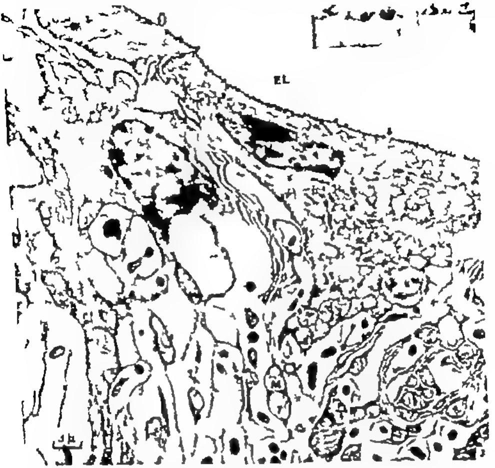

Fig. 2. Survey electron micrograph of the stria vascularis fixed in glutaraldehyde. Final product (arrows) is located on the outer cell membrane facing the endolymphatic space (*EL*). No activity is found anywhere else because glutaraldehyde preserves the integrity of membrane barriers to perfusing solutions. Nucleus (N), mitochondria (*M*). × 9000. The inset shows final product in the plasma membrane facing endolymphatic space at high magnification. × 22,000.

methane maleate (tris-maleate) buffer pH 7.2, 0.5 m*M* Adenosinetriphosphate (disodium salt), 2.0 m*M* lead nitrate, 4.0 m*M* magnesium sulfate and 100.0 m*M* sucrose (final pH 7.1, tonicity 300 milliosmoles) for 5 or 15 minutes at room temperature. When a slight cloudiness occurred the mixture was filtered before use.

After incubation all tissue samples were washed in cold 0.44 Mol sucrose briefly and then fixed additionally in 1% osmium tetroxide buffered to pH 7.2 for 1.5 hours, dehydrated in alcohol and embedded in Epon plastic. Thin sections were cut with an LKB *ultratome*, and mounted on Formvar coated copper grids. These were examined without any additional staining in an RCA EMU 3G electron microscope.

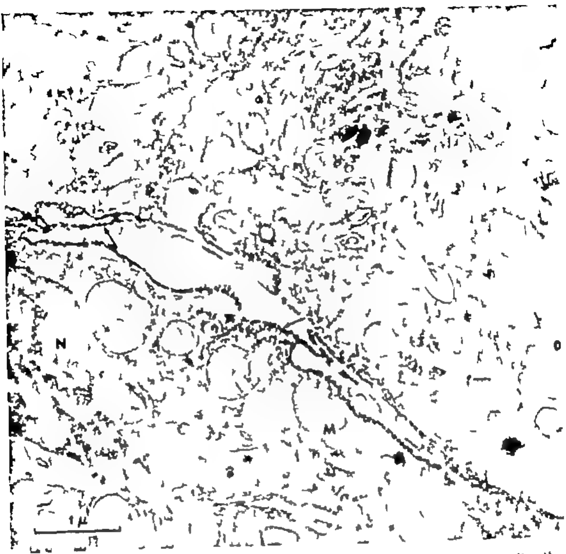

Fig 4 Glutaraldehyde prefixation followed by freezing pe[illegible] Reaction product (arrows) is visible on the folded plasma membranes but mitochondrial ATPase is inhibited by glutaraldehyde Nucleus (N) mitochondria (M) × 20,000

(6) Control specimens were prepared by following each of the procedures as outlined above with the exception that ATP was omitted from the incubation medium

RESULTS

As illustrated in Fig 1 the stria vascularis is a complicated tissue system consisting of three layers of epithelial cells resting on the connective tissue of the spiral ligament The cells facing the endolymph have a denser cytoplasm than the other layers and are known as marginal cells or dark cells The layer next to the spiral ligament is formed by basal cells Between the basal and the marginal cells are the intermediate cells Each type of epithelial cell is characterized by complex cytoplasmic folding

Fig. 3. The stria vascularis following formalin fixation. Final product (arrows) is in the surface membrane and folded plasma membranes. Endolymphatic space (*EL*), nucleus (N) × 14,000

Kikuchi & *Hilding* (1966) recently showed that only the marginal cells appear to be derived from ectoderm, the intermediate and basal cells are probably mesodermal.

The comparative results of different procedures are indicated in the Table 1.

When prefixation was done with osmium tetroxide, reaction precipitate granules were concentrated on the surface membrane and the infolded plasma membrane in the stria vascularis and spiral ligament cells (Fig. 2). There was a variation of results between different experiments using the same procedure. Some of this variability can be accounted for by imperfect penetration of tissue by osmium tetroxide.

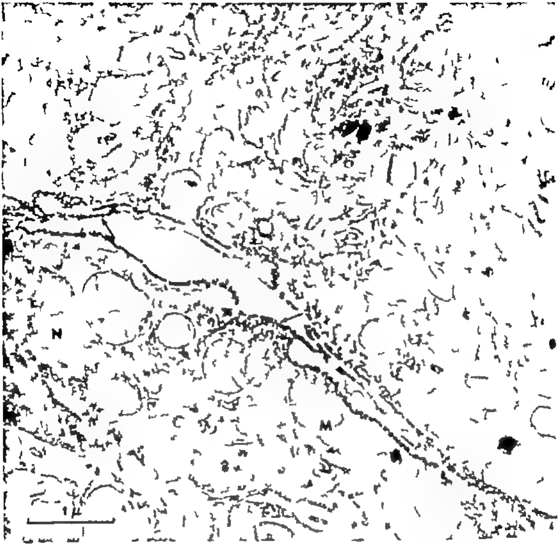

FIG. 4 Glut raldehyd prefixation f ll wed by freezi g p i r to tal ing Reacti n product (arrows) i isible on the f ld d pl ma m mbranes but mitochondrial ATP ase is inhibited by glutaraldehyd Nu l us (N) mitoch ndri (M) 20 000

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Fig. 7. Cross section of a capillary of the stria vascularis, prefixed with formalin. Reaction product is seen on the membranes of the stria vascularis cells surrounding the blood vessel and precipitate (arrow) also appears in the region of the basement membrane (*B*). Reaction product is not present within the endothelial cells (*E*). Vessel lumen (*L*). × 14,000.

Mitochondrial localization of the reaction product in spiral ligament was demonstrated in this procedure (Fig. 6).

In some instances reaction products were seen in the basement membrane region surrounding the capillary (Fig. 7).

It was possible to demonstrate deposition of the reaction products in the mitochondria of the cells of the stria vascularis and spiral ligaments when tissue was incubated in a mixture which consisted of trisaminomethane maleate buffer (pH 7.2), Adenosinetriphosphate (disodium salt), lead nitrate, magnesium sulfate and sucrose for 5 minutes at room temperature without any prefixation. These deposits were sometimes confirmed to the mitochondrial membranes, but, in other instances, reaction products were irregularly distributed in the mitochondrial matrix. In addition to the activity in the mitochondria, activity appeared on the surfaces between adjacent marginal cells (Figs. 8 and 9). No reaction deposit was seen in the infolding cell membranes and the basement membranes of capillaries after short incubation (*5 min.*).

When the material incubated for a longer time (15 min.) reaction deposit was seen in the cell membranes and the mitochondria. However preservation of fine structure was poor (Figs. *10* and *11*).

In control specimens incubated in medium from which ATP was omitted, metal precipitates were entirely absent.

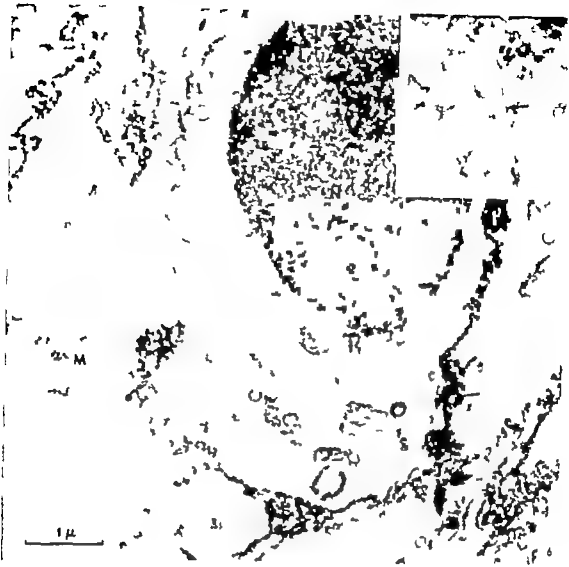

FIG. 6 Spiral ligament Formalin prefixation. Mitochondrial localization of the reaction product is demonstrated. Nucleus (N) mitochondria (M) × 13,000 The inset × 500,000

Tissue that was fixed in glutaraldehyde for 30 minutes and then incubated with the substrate prior to further osmium fixation was well preserved

Localization of the reaction product in the outer cell membranes facing the inner ear fluid space was well demonstrated by this method but no activity was found within the cells of the stria vascularis and spiral ligament (Fig 3)

Reaction deposits in the infolding plasma membrane in the stria vascularis and spiral ligament were seen if the tissue was frozen prior to staining However some damage of fine structure in the tissue could not be avoided (Fig 4)

In tissue on which formalin sucrose was used as prefixation a dense reaction product was found in the surface membrane and infolded plasma membrane of the stria vascularis and spiral ligament cells (Fig 5)

Fig. 9 Higher magnification of part of (Fig. 7). The reaction product (arrows) is present in the cristae and outer membrane of mitochondria (*M*) and the interfaces of the opposed membranes of marginal cells. 33,000

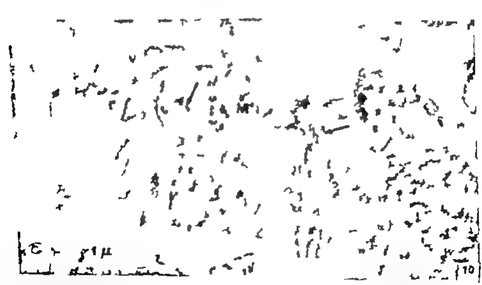

Fig. 10 Part of marginal cell incubated for fifteen minutes with no prefixation. The final product (arrows) is present in the mitochondria (*M*) and infolded plasma membrane. 33,000.

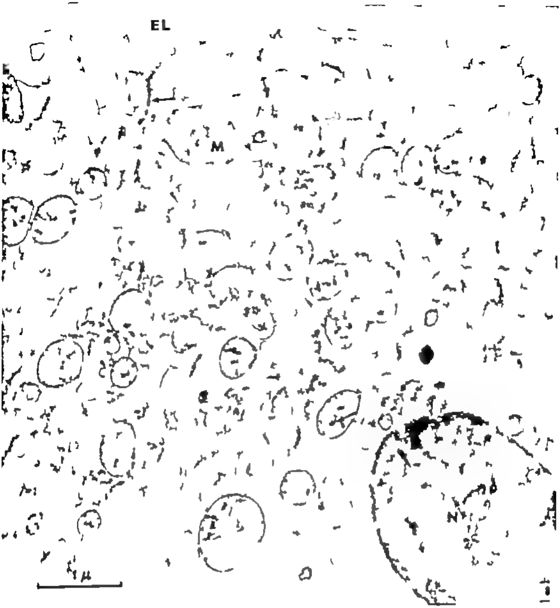

Fig 8. M la vasculari incubated f o ly M minutes after no prefi ll While reaction product (arrows) can be identified in mitochondria (M) mo t of the f lded pl sma m mbra e) no reacti e 16,000

When β glycerophosphate or Adenosine-5 monophosphate was used as substrate the tissues were also unreactive. Sparse deposits were found in some areas but these bore no constant relationship to cellular components (Figs 12 and 13)

DISCUSSION

The purpose of this study was to reach a better understanding of the way in which ATP ase is distributed in the stria vascularis because ATP ase is an enzyme thought to be important in fluid transport Light microscopy was found to be inadequate so a histochemical method had to be

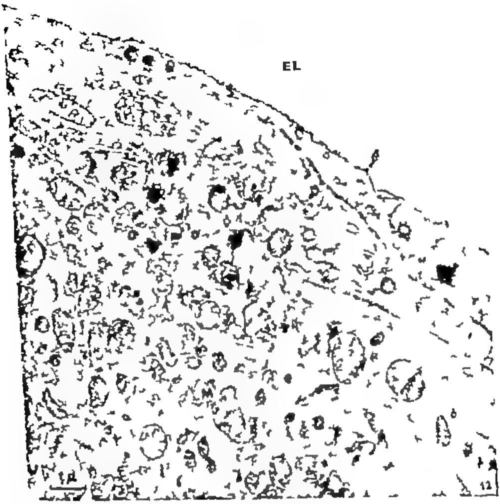

Fig. 12. Control preparations. The stri ascularl incubated without ATP N reaction product is visibl   10,000

d hyde is regarded as a superl tive fixative because fine membranes and structures are well preserved. This admirable quality of a fixative appears t interfere with its use a a pre-fixative before histochemistry for the well-preserved membranes inhibit the penetration of reagents.

Koide, Hando & Yoshikawa (1964) pointed out the existence of a barrier between the endolymphatic space and stria vascularis which interferes with precise observation of the distribution of succinic dehydrogenase and DPN-diaphorase. They showed that a freezing method seemed pre ferabl because it broken the integrity of membranes. The plasma membrane f the marginal cells is thicker on th endolymphatic surface than on other part of the cell (Echandia & Burgos, 1965)

W found that freezing after fixation with glutaraldehyd disrupted

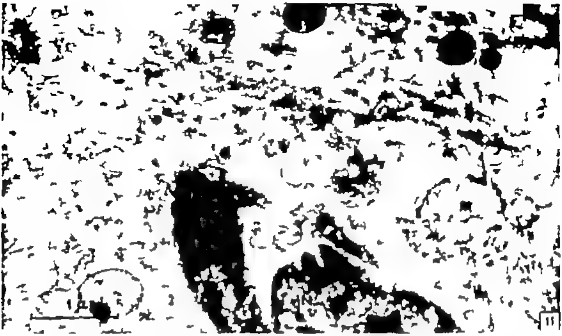

FIG. 11 Spiral ligam nt incubated f r fift en minute with no prefixation The reaction product (arrows) is seen in mitochondria (M) nd the plasma membrane 20,000

developed for electron microscopy which would be suitable for the inner ear

As Torack (1965) so succinctly stated "Fixation is a necessary evil in many histochemical techniques demonstrating enzyme activity However if its destructive aspect can be characterized and reproduced there appears to be no reason why a method of fixation cannot contribute to the speci ficity of an enzyme reaction " The way ATP-ase activity appears at various sites in the stria vascularis and spiral ligament depending on the method of fixation suggests that a different effect on the enzyme has been produced by each of these fixatives However we found that a given fixative would produce a reproducible pattern each time the reaction was tried Although gradient effects of fixation can never be completely eliminated uniformity was observed if sufficient time was allowed for the fixative to thoroughly penetrate the tissue

The aldehydes and osmium tetroxide differ in their effects on the ultra structural demonstration of adenosine triphosphatase in the stria vascularis and spiral ligament The most general localizing of reaction deposits is observed with formalin fixation but more care is required to obtain intact fine structure This fixative is recommended for studying the overall distribution of this enzyme The use glutaraldehyde provides excellent ultrastructure but the least evidence of surviving enzymatic activity (Torack & Barrnett 1964 Barrnett 1964 Marchesi Sears & Barrnett 1964 Sabatini Miller & Barrnett 1964) In this study no reaction product was seen except on the cell membranes facing endolymph and perilymphatic spaces This phenomenon could mean that the reagents do not penetrate the surface of the stria vascularis after glutaraldehyde fixation Glutaral

Fig. 12 Control preparations. The stria vascularis incubated without ATP. No reaction product is visible. × 16,000

dehyde is regarded as a superlative fixative because fine membranes and structures are well preserved. This admirable quality of a fixative appears to interfere with its use as a pre fixative before histochemistry for the well-preserved membranes inhibit the penetration of reagents.

Koide, Hando & Yoshikawa (1964) pointed out the existence of a barrier between the endolymph tic space and stria vascularis which interferes with precise observation of the distribution of succinic dehydrogenase and DPN-diaphorase. They showed that a freezing method seemed preferable because it broken the integrity of membranes. The plasma membrane of the marginal cells is thicker on the endolymphatic surface than on other part of the cell (Echandia & Burgos, 1965)

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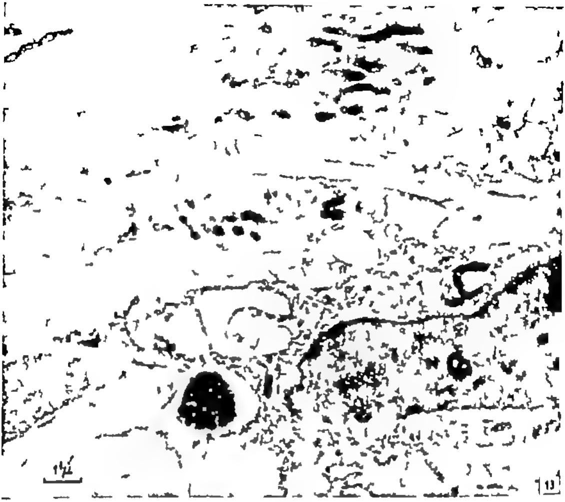

FIG. 13 The spinal ligament incubated with ut ATP N reacti n product i vi ible n tl plasma membrane and mitoch ndria 10 000

these thick membranes and reaction product could then found generally on all surfaces of the epithelial cells (Fig 4) Much better preservation resulted when osmium fixed tissue blocks were used However extensive lo s of enzyme activity is produced by this fixation An estimate of the residual enzyme activity which remain in the tissue blocks exposed to osmium tetroxide for brief time is given by Essner Novikoff & Masek (1958) When assayed in the Wachstein Meisel medium there is about 15 per cent survival of the ATPase activity It is thus to be expected that osmium tetroxide for prefixation would have limited applicability However in the infolding plasma membrane of the stria vascularis sufficient enzyme activities survives for abundant producti n of lead phosphate deposition (Fig 2)

Previous investigators have demonstrated histochemical and biochemical differences among enzymes capable of hydrolyzing adenosine triph phate at physiological pH in other tis ues (Essner Novikoff & Ma ek 1958 Post *et al.*, 1960 Duel & McIlwain 1961 Hess, 1962 Allen 1963 Novik ff & Hess 1963)

Chemical studies on cell fractions have indicated that ATPase is present

predominantly in mitochondria in other tissues. The demonstration of ATP-ase in mitochondria is of considerable interest, since this had not been accomplished until the recent study of Wachstein, Bradshaw & Ortiz (1962) They used light microscopy and found ATP-ase activity in mitochondria Apparently one of the difficulties in the fine localization on the cristae which would be difficult or impossible to see with light microscopy In our material fixed in formol-sucrose solution prior to incubation, reaction product occurred on the cristae of mitochondria in the spiral ligament. Also using Macheal s modification (1966) of the Wachstein–Meisel medium with no prefixation localization of the reaction product in mitochondria in the stria vascularis and spiral ligament was seen When the tissue was incubated in reaction medium without any prefixation, in incubation time had to be shortened to preserve fine structure Five minutes incubation time was suitable for demonstrating mitochondrial ATP ase Although reaction product occurred in mitochondria and cell membrane in tissues incubated for a longer time preservation of fine structure in mitochondria was poor

Localization of reaction product of ATP ase on the cristae and membranes of mitochondria is in accord with chemical demonstration of enzyme in mitochondria fractions obtained by ultracentrifugation of cell homog nates (Padykula & Herman, 1955) Siekevitz, *et al* (1958) have suggested a possible role for mitochondrial ATP-ase in oxidative phosphorylation. We hav recently studied the pattern of a distribution of succinic dehydrogenase and cytochrome oxydase in mitochondria and found localization of this enzyme on the mitochondrial cristae

ATP-ase activity was localized in the basement membrane of the capillaries of the stria vascularis when formalin sucrose solution was used for prefixation. Using aldehyde prefixation, Torack Benson & Becker (1961) found that this enzyme activity appeared in the basement membrane and glial nd feet about the capillaries of the cerebral cortex.

As several have pointed out, the complicated folding pattern of the stria vascularis cells resembles fluid transport cells in the pancreas, salivary glands and kidney (Engström, Sjöstrand & Spoendlin, 1955 Smith, 1957 Echandia & Burgos, 1965 Kikuchi & Hilding, 1966) ATP-ase activity has been correlated with this type of cell structur in other organs Similarly in th fenestrated capillaries t the base of the renal tubules, enzyme activity was lacking in the endothelial cells but was present at the surface membran of the basal infoldings *of the* tubular epithelium (Ashworth, Luibel & Stewart, 1963 Nakai, 1965) This latter situation frequently has been found in transport phen mena.

SUMMARY AND CONCLUSIONS

Th distribution of ATP-ase activity wa studied by electron microscopy Several procedures were tried u ing glutaraldehyde formaldehyde or

osmium tetroxide for prefixation Freezing broke down membranous bar riers to infiltration of the tissue by reagents

The reaction product appeared on the cell membranes and basement membranes of blood vessels in the stria vascularis and spiral ligament Precipitate was particularly obvious on the cell membrane facing the endolymphatic space in the stria vascularis The cell membrane of the spiral prominence and infolding plasma membrane in the stria vascularis was also very active

ATP-ase localization in the mitochondria was also demonstrated Each method of prefixation produced a somewhat different localization for various reasons yet a definite pattern emerged As has been proved by biochemical studies, mitochondria are rich in this type of enzyme activity The *surfaces of all kinds of cells in the stria vascularis* showed activity when conditions were favorable

In general our results could have been predicted by comparison with the results with other fluid transport tissue Therefore they fully support the notion that the stria vascularis is important in endolymph metabolism We expect to utilize this histochemical techniques to improve our evaluation of the pathological stria vascularis in Ménière s syndrome.

ZUSAMMENFASSUNG

Der zytochemische Nachweis von Adenosintriphosphatase-Aktivität in der Stria vascularis und des Ligamentum spirale in der Cochlea wurde mit verschiedenen Techniken der Elektronenmikroskopie studiert. Die ATP-ase-Aktivität wurde an den Oberflächen der komplizierten fingerförmigen Fortsätze zwischen den epithelialen Zellen und an den Zellmembranen im endolymphatischen Raum gefunden *Die Basalmembran der Kapillaren und die Mitochondrien zeigen* auch deutliche enzymatische Aktivität Diese Befunde weisen einige Kennzeichen auf die vielleicht sekretorische und absorptive Prozesse andeuten Die Bedeutung der Resultate wird diskutiert.

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ELICITATION OF HORIZONTAL NYSTAGMUS BY PERIODIC LINEAR ACCELERATION

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Four subjects in each of four different body orientations were exposed to periodic linear acceleration stimuli produced by simple harmonic translation of 0.2, 0.4 and 0.8 cps cyclic frequency along an Earth horizontal axis. Highly systematic horizontal nystagmus was demonstrated in response to these stimuli as well as to linear acceleration of rotating vector form equivalent to counterrotation in a constant magnitude linear force field. Vertical nystagmus could not be demonstrated for similar stimuli. The peak velocity of the slow component of nystagmus and the phase lag of the nystagmoid response behind the linear acceleration stimulus were found to differ from those associated with periodic angular stimulation of the semicircular canals in a comparable frequency range. Regardless of stimulus form, the effective stimulus element for elicitation of horizontal nystagmus appeared to be dynamic change in the linear acceleration component directed along the subject's y (left–right) head axis.

INTRODUCTION

In general, it has been accepted that the semicircular canals serve as the primary biological transducer for angular motions, while the otolith mechanisms are considered to be the equivalent sensor for linear acceleration stimuli. Experimentation in the vestibular field has been such, however, that a great deal more data are available to describe the response behavior of the semicircular canals than of the otolith mechanism. It has been shown (Hixson & Niven, 1961) how frequency response analysis techniques making use of sinusoidal angular accelerations of varying frequency and magnitude as stimuli and ocular nystagmus as a physiologically objective response may be applied to the quantification of the performance characteristics of the semicircular canals.

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The presentation of dynamic linear acceleration stimuli fully independent of potential angular acceleration effects is more difficult, and few studies have been performed Nonreversing eye movements of nystagmic form have been reported in experiments using vertical oscillators (McCabe 1964) parallel swings and horizontally accelerated carts (Jongkees & Philipszoon, 1962) Guedry (1964) using a horizontal axis rotator obtained a non reversing nystagmus of long duration during constant velocity rotation and suggested that it was dependent upon a continuous reorientation of the otolith system relative to gravity Benson & Bodin (1965) using similar stimulation obtained similar results but attributed it to direct action of the 1 g rotating linear acceleration vector on the canal system, although they did not positively exclude otolithic effects

The demonstration of a highly systematic nystagmus unequivocally keyed to changes in both direction and magnitude of linear accelerations in the absence of potentially confounding angular accelerations would be of obvious practical and heuristic value

PROCEDURE

Subjects

Four males with no apparent defects in hearing or equilibrium served as subjects Three of the subjects (the authors) had previous experience on the device, and all were acquainted with the procedure and objectives of the experiment

Apparatus

Linear acceleration stimuli were generated by the Coriolis Acceleration Platform (CAP) to be described in detail elsewhere (Hixson & Anderson, 1966) This device consists of a cylindrical capsule 20 feet in diameter centered on the rotational axis of the device and a 40-foot horizontal track superstructure extending through the room and projecting outward on both sides A subject carrier on the track is coupled to a position servo-mechanism drive system which can be programmed to produce sinusoidal linear motions with peak ratings of ± 20 ft displacement, ± 16 ft/sec velocity ± 3 g acceleration, and 1 cps frequency For the present experiment, the subject carrier was a 4 foot cubical cab which could be statically rotated about any of its three axes to preposition the subject relative to the acting linear acceleration

A triaxial linear accelerometer positioned at the subject s head level was used to measure the linear acceleration stimulus A high gain preamplifier for physiological recording was also located within the cab Direct-current corneoretinal potentials reflecting horizontal and vertical eye displacements were amplified filtered and recorded on an 8-channel direct writing recorder located in a nearby control room

TABLE 1 *Comparison of actual and normalized magnitudes of three linear acceleration stimuli*

Motion parameter	Stimulus No. 1		Stimulus No. 2		Stimulus No. 3	
	Actual	Normalized	Actual	Normalized	Actual	Normalized
Frequency (cps)	0.2	1	0.4	2	0.8	4
Peak displacement (ft)	±11.78	1	± 2.94	0.25	± 0.74	0.06
Peak velocity (ft/sec)	±14.77	1	± 7.38	0.50	± 3.69	0.25
Peak acceleration (ft/sec²)	±18.56	1	±18.56	1	±18.56	1

Experimental Stimuli

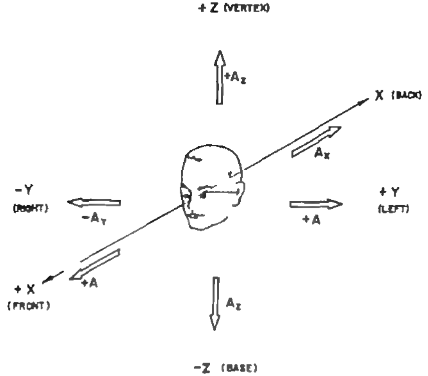
The stimuli consisted of three oscillations of variable frequency and constant magnitude peak acceleration. The frequencies were 0.2, 0.4 and 0.8 cps, and the peak track displacement was adjusted to maintain the peak acceleration level constant at 18.6 ft/sec² (0.58 g) for all frequencies. The actual and normalized characteristics of the stimuli are presented in Table 1 where each parameter is normalized relative to its value at 0.2 cps.

Experimental Method

Each subject was exposed to each of the three frequencies while oriented in four positions relative to the direction of the linear acceleration vector. The kinematic notation for the stimulus is summarized in graphic and equation form in Fig. 1. The, x, y and z head axes denote the front-back, left-right, and vertex-base dimensions, respectively, of the skull while the frontal, sagittal, and horizontal head planes are identified as the yz, xz, xy planes of the head, respectively. The components of the resultant linear acceleration of the head acting along the x, y and z head axes are denoted as A_x, A_y, and A_z respectively in the directional sense denoted in Fig. 1.

The four basic orientations used in this study included: Mode 1, the subject lying on his back and oriented so that the sagittal xz head plane was at right angles to the direction of the linear track motions. Mode 2, same as Mode 1 except subject sitting upright. Mode 3, the subject lying on his back with his horizontal xy head plane at right angles to the track motion. Mode 4, the subject sitting in an upright position with his frontal yz head plane normal to the track motions.

Two subjects were presented the stimulus frequencies in an ascending order and two in a descending order. For one subject of each pair horizontal and vertical nystagmus were first recorded with eyes closed, then with eyes open; for the other the recording sequence was reversed. The subject was instructed to maintain a straight-ahead gaze at all times during cab oscillation with his head rigidly fixed by means of an individual,



FRONTAL PLANE	SAGITTAL PLANE	HORIZONTAL PLANE
A |A |∠ϕ_a	A_{xz} |$\bar{A}_{xz}$|∠ϕ	A |A_{xy}|∠ϕ
|$\bar{A}$ | (A A)	|$\bar{A}_{xz}$| (A A)$^{1/2}$	|$\bar{A}_{xy}$| (A A_x)$^{1/2}$
ϕ ARC TAN(-A /A)	ϕ ARC TAN (A /A)	ϕ ARC TAN(A /A)

FIG. 1 Sch matic di gra i gi l g ba ic n tati n in pict ial nd eq ati form f r the lin a acceleration timuli ting n the subject

custom molded plaster cast and with his body fixed securely to the seat by straps.

Nystagmus recording circuits were calibrated by having the subject fixate alternately two target points of known angular separation After calibration the experimental cab was closed light tight and the subject was oscillated at one of the test frequencies Recording was delayed for 60 seconds to minimize biological transient effects the subject was then instructed to open or close his eyes as the experimental conditions required, and eye motions were recorded for 60 seconds Chatter and performance of mental arithmetic were used to encourage maximal nystagmic response A rest period of at least 2 minutes was allowed before the next experi mental run

The procedure was then repeated with the subjects instructed to view a 7 $^1/_2$ inch by $^1/_{32}$ inch luminous line target (aligned with the axis in Modes 1 and 2 with the y axis in Modes 3 and 4) and report their impres sions of target movement On the trials with eyes closed reports of postural sensations were obtained

RESULTS

Horizontal nystagmus was elicited by the periodic linear acceleration stimulus in certain body orientations. Recordings of horizontal nystagmus obtained when the resultant of the track and gravitational accelerations was acting in the horizontal plane of the head (Mode 1 orientation) with the eyes open are reproduced in Fig. 2 A. Essentially similar responses were obtained in the eyes closed condition. A pronounced horizontal nystagmus was also observed when the resultant acceleration vector was varied in the frontal plane of the head (Mode 2 orientation) as may be seen in Fig. 2 B. Neither horizontal nor vertical nystagmus could be observed in the Modes 3 and 4 orientations (see Fig. 3).

The nystagmus obtained in Modes 1 and 2 orientations was analyzed to determine phase shift and magnitude of peak slow component eye velocity. The phase lag of the nystagmic response was measured as the interval between the transition in acceleration direction (zero acceleration) and the transition in direction of the slow component of the nystagmus (zero eye velocity). This method has been described in detail in an earlier report (Niven & Hixson, 1961). Peak slow component velocity was determined by measuring the slope of the individual nystagmic responses during each cycle and selecting the maximum value. A summary of the result is presented in Table 2. The subject means contained in Table 2 were obtained by combining the values obtained for eyes open and eyes closed for body orientations Modes 1 and 2. Lack of any statistical difference between these conditions permitted this grouping.

Postural and Visual Subjective Sensations

The visual impressions of the luminous line target may be summarized as follows. During Modes 1 and 2 stimulation the line target remained directly ahead of the subject for all experimental frequencies. The visual target had predominantly the quality of apparent velocity, that is, it appeared to move with the observer as he experienced movement to the left or right. Apparent displacement, that is, lag or lead of the sensation of postural displacement by the target, or apparent tilting of the target clockwise or counterclockwise, was either not observed or was minimal. During Modes 3 and 4 stimulation, as in the case of the other two body orientations, the target remained directly ahead of the subject and moved back and forth with him. However it did not appear to be displaced above or below the subject at any time during the test trials.

The postural sensations may be summarized as follows. In Modes 1 and 2 the subject perceived primarily a pure translation or side-to-side motion of the body. In Modes 3 and 4 the sensations were similarly of fore-and-aft displacement along the track. In a number of instances, there was a tendency to report a brief yawing, rolling, or pitching sensation, depend

ing upon orientation at the point of maximum displacement but generally the sensations were described as simple translatory movements

DISCUSSION

The eye motion recordings of this study show clearly that linear acceleration is an adequate stimulus to produce nystagmus This horizontal nystagmus appeared whenever the head was oriented with its sagittal x plane at right angles to the direction of the track accelerations. In effect horizontal nystagmus resulted when the y (left–right) head axis was aligned with the direction of motion for both the erect and supine postures. Horizontal nystagmus was not observed for the orientations where the *track acceleration acted at right angles to either the frontal y or horizontal xy* head planes, i e., for accelerations directed along the x and head axes, respectively where $A_y = 0$

In contrast vertical nystagmus was not seen under any of the four stimulus conditions of the study even with greatly increased recording sensitivity During various related pilot studies other body orientations which involved statically tilting the three cardinal head planes relative to the direction of motion were used In no case was vertical nystagmus recorded At most there sometimes occurred *sinusoidal variations of the* baseline which had little repeatable correlation with the amplitude-time profile of the stimulus

The characteristics of the observed horizontal nystagmus and its relationship to the linear acceleration A_y acting along the y head axis can be summarized as follows Each change in direction of the A_y stimulus was accompanied by a change in direction of the slow component of eye velocity The time-course of these changes was such that the reversals in the direction of *nystagmus lagged slightly behind the reversals in the direction of* the A_y stimulus Acceleration to the left produced nystagmus with the slow component of eye velocity to the right and vice versa The instantaneous slow component of eye velocity described a sinusoidal waveform closely resembling that of the sinusoidal A stimulus

The frequency dependence of the nystagmus data as derived from a magnitude and phase analysis of the slow component of eye velocity (Table 2) can be described as follows The mean peak eye velocity remained *constant at approximately 10 deg/sec at $F = 0.2$ 0.4* and 0.8 cps so that this parameter can be considered independent of frequency over the denoted stimulus range The directional transitions in eye velocity showed a relatively small increase in *phase lag as the stimulus frequency* was increased i e mean phase angles of approximately 26 31 and 38 at 0.2 0.4 and 0.8 cps, respectively

With the three stimulus configurations chosen for this study frequency served as the independent variable with the condition that the peak acceleration was held constant through ut As indicated by the normalized magnitude data of Table 1 when the stimulus frequency was raised from

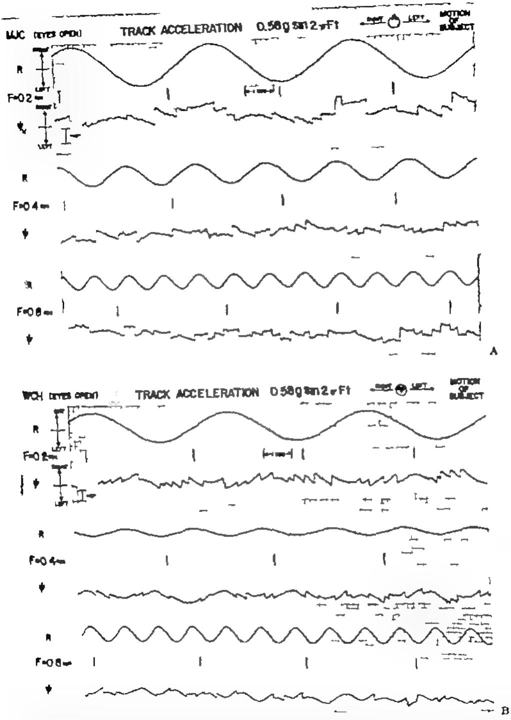


FIG. 2. Horizontal nystagmus recorded at three different stimulus frequencies. The sinusoidal waveform identified as R in each record describes the instantaneous displacement of the subject. (A) The track acceleration component is directed along the y head axis of the subject while lying on his back (Mode 1). (B) The track acceleration component is again directed along the y head axis although he is seated erect (Mode 2).

0.2 to 0.8 cps (a fourfold increase) the peak velocity and peak displacement were reduced to $^1/_4$ and $^1/_{16}$, respectively, of their values at 0.2 cps. Thus the peak value of the slow component of eye velocity, which remained relatively constant, is keyed to the acceleration parameter rather than to the velocity or displacement parameters of the simple harmonic motion stimulus.

One further observation involves the decay time of the nystagmus following cessation of the stimulus. The experimental procedure was such that upon completion of the nystagmus recording sequence the track carriage was stopped within 2 to 5 seconds. The decay of the nystagmus was so rapid that its termination was almost coincidental with termination of the stimulus. This observation combined with the constant peak amplitude and minimal phase shift data observed over the relatively high stimulus frequency region indicates that the biological sensing mechanism or mechanisms responsible for the nystagmus have a relatively fast response time when stimulated in this fashion.

The data arose from a stimulus condition in which a linear acceleration vector of variable magnitude acted along a single fixed morphological axis. Horizontal nystagmus has also been induced in pilot studies of two subjects exposed to a counterrotation type stimulus defined by an Earth horizontal, linear acceleration vector of constant magnitude rotating at constant angular velocity in a given morphological plane. This stimulus was produced by linearly oscillating the track platform at constant frequency ω rad/sec while simultaneously rotating CAP at constant angular velocity $\dot{\Theta}$ rad/sec with the special condition that ω was identical to $\dot{\Theta}$. Also by varying the peak track displacement while holding track frequency and rotational velocity constant and equal, it was possible to obtain different constant magnitude levels of the rotating linear acceleration vector.

A record presented in Fig. 4 shows the horizontal nystagmus produced by rotation of such a linear acceleration vector through the horizontal xy head plane. The resultant nystagmus is characterized by periodic reversals in direction and a slow component of eye velocity which is of sinusoidal waveform. Moreover, the nystagmus is keyed to the component of the stimulus acting along the y head axis. This component, A_y, is fully equivalent to that produced by the simple harmonic translation stimulus since it is of sinusoidal waveform.

For both subjects each reversal in direction of horizontal nystagmus followed closely the reversal in direction of A_y; acceleration to the right produced nystagmus with a *slow component to the left, and vice versa*. (The phase relationship between the nystagmus and A_y can be observed in Fig. 4 by noting that A_y has a waveform identical to that of the stimulus reference channel shown, but with a 90-degree phase lag.) In essence the nystagmus elicited by linear acceleration generated through counterrotation was similar to that elicited by harmonic translation along the y head axis.

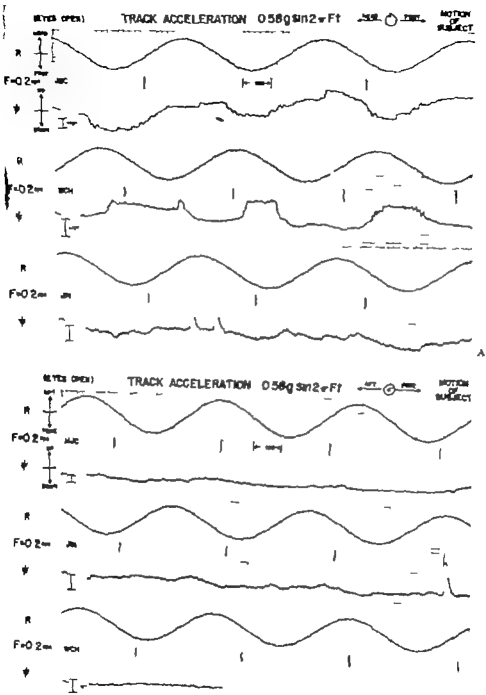


Fig. 3. Vertical ey mov ment recorded ith the track acceleration directed along the head (Mode 3 box) and the head xis (Mode 4 below). The absence of ertical nystagmus i in marked contrast with the horizontal nyst gmus licited by y xis stimulation. B

0.2 to 0.8 cps (a fourfold increase) the peak velocity and peak displacement were reduced to $^1/_4$ and $^1/_{16}$ respectively of their values at 0.2 cps. Thus the peak value of the slow component of eye velocity which remained relatively constant is keyed to the acceleration parameter rather than to the velocity or displacement parameters of the simple harmonic motion stimulus.

One further observation involves the decay time of the nystagmus following cessation of the stimulus. The experimental procedure was such that upon completion of the nystagmus recording sequence the track carriage was stopped within 2 to 5 seconds. The decay of the nystagmus was so rapid that its termination was *almost coincidental with termination of* the stimulus. This observation combined with the constant peak amplitude and minimal phase shift data observed over the relatively high stimulus frequency region indicates that the biological sensing mechanism or mechanisms responsible for the nystagmus have a relatively fast response time when stimulated in this fashion.

The data arose from a stimulus condition in which a linear acceleration vector of variable magnitude acted along a single fixed morphological axis. Horizontal nystagmus has also been induced in pilot studies of two subjects exposed to a counterrotation type stimulus defined by an Earth horizontal *linear acceleration vector of constant magnitude rotating at constant* angular velocity in a given morphological plane. This stimulus was produced by linearly oscillating the track platform at constant frequency ω rad/sec while simultaneously rotating CAP at constant angular velocity Θ rad/sec with the special condition that ω was identical to Θ. Also by varying the peak track displacement while holding track frequency and rotational velocity constant and equal it was possible to obtain different constant magnitude levels of the rotating linear acceleration vector.

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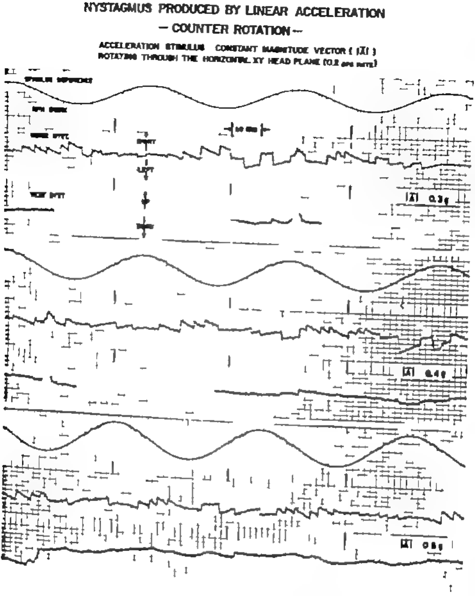

Fig. 4 Horizontal nystagmus produced by rotation of a constant magnitude linear acceleration vector through the horizontal xy head plane. The stimulus is equivalent to counterrotation of a subject at a constant angular velocity in a centripetal acceleration field of 0.3, 0.4, and 0.5 g, as denoted at the right of each recording. The reversals in the direction of the slow phase of nystagmus are keyed to the reversal in direction of linear acceleration component acting along the y head axis which occurs at the instant of maximum displacement on the stimulus reference curve.

TABLE 2. *Mean of peak slow component velocity* ($\dot\psi$) *and phase shift angle* (ϕ) *of ocular nystagmus as a function of the frequency of a sinusoidal linear acceleration stimulus*

n = number of measurements on which mean is based

	Frequency (cps)					
	0.2		0.4		0.8	
Subject	$\dot\psi$ (deg/sec)	ϕ (deg)	$\dot\psi$ (deg/sec)	ϕ (deg)	$\dot\psi$ (deg/sec)	ϕ (deg)
MJC	9.16	23.10	7.81	20.01	17	30.25
n	[illegible]	78	51	66	18	50
JFG	8.00	27.60	7.20	40.20	89	30.47
n	15	48	31	31	23	12
WCH	11.01	2 11	12.81	32.08	16.31	17.57
n	51	56	61	—	21	59
JIN	5.33	3.72	7.09	22.08	0.32	21.38
n	21	28	18	6	20	6
Group mean	0.20	25.00	0.01	31.18	0.33	[illegible].01
n	107	210	170	183	115	127
Pooled s.d.	3.03	9.38	2.50	11.12	2.89	16.01

The nystagmus of this study also closely resembles that recorded when a subject is exposed to sinusoidal angular acceleration of variable frequency about an Earth vertical axis. In the latter case each reversal in direction of the angular acceleration stimulus is accompanied by a reversal in the direction of the nystagmus with a yaw acceleration to the subject's right (about the head axis) leading to nystagmus with a slow component of eye velocity to the left and vice versa. In addition the waveform of the instantaneous magnitude of the slow component of eye velocity follows the sinusoidal waveform of the angular acceleration stimulus.

However, two important differences in nystagmus characteristics result for the two stimulus conditions. For sinusoidal angular accelerations in the vicinity of 0.2 cps, it has been shown that the directional nystagmus transitions lag the driving angular acceleration or torque producing the response by 80 to 90 degrees (Hixson & Niven 1962, Niven & Hixson 1961). Further, the peak magnitude of the slow component of eye velocity decreases as the frequency is raised. In general the magnitude and phase characteristics of the slow component of eye velocity for frequencies near and above 0.2 cps are such that sinusoidal angular oscillations of constant peak velocity form tend to produce constant peak velocity nystagmus; for frequencies far below 0.2 cps, oscillations of constant peak acceleration form tend to produce a nystagmus with constant peak velocity. That is to say, the transduction processes are frequency dependent, keyed to acceleration at very low frequencies and to velocity at the higher frequencies. In the same context the nystagmus elicited by sinusoidal linear

feasible to specify the responsible biological sensing system, e.g. otolith or canal receptors.

ZUSAMMENFASSUNG

Vier Versuchspersonen wurden jew ils in vier verschiedenen Körperorientierungen periodischen linearen Beschleunigungsreizen ausgesetzt, die mittels einfacher harmonischer Translation von 0,2 0,4 und 0,8 zyklischer Frequenz längs einer erdhorizontalen Achse erzeugt wurden. Äusserst systematisch konnt horizontaler Nystagmu demonstriert werd n als Reaktion uf diese R ize sowohl al auch uf linear Beschleunigungen von rotierender Vektorform äquivalent mit Gegenrotation in einem linearen Kraftfeld konstanter Grösse. Vertikaler Nystagmus konnte nicht demonstriert werden für gleiche Reiz. Es wurde gefunden, dass die Grösse d langsamen Komponente der Augengeschwindigkeit und ihrer Phasenverschiebung hinter dem linearen Beschleu igungsreiz verschied n sind on denen die bei periodischen Drehreizen der Bogengänge in inem vergleichbaren Frequenzbereich auftreten. Unabhängig von der Form des Reizes schien da wirksame Reizelement für die Auslösung des horizontalen Nystagmu der dynamische Wechsel der li earen Beschleunigungskomponent in Richtung der *y* (links–recht) Kopfa hse der Versuchsperson zu sein.

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accelerations becomes analog to an acceleration transduction process in the 0.2 to 0.8 cps stimulus range since no change in nystagmus peak velocity occurred. This mode of response will not, however, extend to very low frequencies since in the limit, i.e., in the static acceleration environment, nystagmus becomes nonexistent. It may be concluded that a dynamic change in acceleration, i.e., jerk, along the *y* head axis is required to elicit the nystagmus.

A comparable interpretation of the visual and postural illusions can be made. It may be noted that the direction of the resultant of the track and gravitational accelerations was changing continuously during each oscillation cycle. With the peak track acceleration of 0.58 *g* the maximum deviation of the resultant linear acceleration vector from Earth vertical was 30 degrees and occurred at the instant of peak displacement to either side of the oscillation center. The stimulus was, however, perceived primarily as translatory motion and not as body tilt. Conversely, when a static linear acceleration vector is reoriented relative to the body, as in centrifuge experiments, the stimulus is perceived primarily as body tilt. It may be hypothesized that perception of body tilt is frequency dependent. When the morphological orientation of a linear acceleration stimulus is changed rapidly, a sensation of motion arises; when changed slowly or held constant, a sensation of tilt arises.

It is clear that studies performed on centrifuge type research devices must consider that dynamic variations in the linear acceleration element of the over-all vestibular stimulus can contribute to the magnitude and direction of the horizontal nystagmus response. More specifically, time variations of the component of the resultant linear acceleration which acts along the *y* head axis, whether due to *magnitude* changes in centripetal, tangential, or linear Coriolis accelerations or to morphological *directional* changes of the same accelerations as well as of the gravitational field itself, may elicit horizontal nystagmus. Further, the nystagmus elicited by such stimuli will act in concert or in opposition to the horizontal nystagmus produced concurrently by the angular acceleration element of the environment and lead to either an attenuation or amplification of the over-all nystagmus response.

These data demonstrate definitively the production of a systematic horizontal ocular nystagmus in response to a dynamic change in linear acceleration acting along the *y* head axis. The response or decay time characteristics as well as the phase and magnitude characteristics of the nystagmic response to periodic linear acceleration differ markedly from those of the comparable response to periodic angular accelerations. However, these differences neither prove nor disprove that the horizontal semicircular canals acting in a physical mode not identical to the classical concept of cupula-endolymph flow respond to periodic linear acceleration stimulation. More studies, particularly on the response to low frequency, high level linear acceleration stimuli, will be required before it becomes

As a subject's report of the duration of an after-sensation is an integral part of the cupulometric test of van Egmond Groen & Jongkees (1948) and other clinical and experimental investigations of vestibular function, a knowledge of the manner in which the post rotational sensation is modified by instruction would clearly be of value.

METHOD

Apparatus

The electric servo-controlled turntable and associated equipment used in this experiment have been fully described previously (Benson, 1962). The subject sat on the turntable with his head stabilized by a dental bite in a vertical position close to the axis of rotation.

Horizontal nystagmus was recorded by a conventional electro-oculographic technique using a DC amplifier and photographic galvanometer recorder. Opaque goggles were worn and the subject was instructed to keep his eyes closed.

Skin resistance was measured between a dry silver electrode, 1 cm in diameter, placed on the ball of the left thumb and a silver plate moistened with conductive jelly placed on the volar surface of the ipsilateral forearm.

The duration of the after-sensation was obtained with an accuracy of ±0.05 sec, from a signal marker operated by the subject, on the galvanometer record.

Conduct of Experiment

The experiment was performed in two phases, separated from one another by at least 14 days. In Phase I all subjects received the same *weak* instructions. Apart from a general description of the test procedure, they were told how the sensation of turning, produced by the sudden stopping of the turntable, would gradually fade away and they were asked to press a signalling button "when you think that the sensation of turning has stopped". An effort was made to maintain the same unemphatic tone of voice for all the subjects.

Subsequently each subject was exposed to eight rotational stimuli, each of which involved acceleration of the turntable at 1°/sec² to a constant speed, which was maintained for 60 sec before rotation was stopped in 0.5 sec. Turntable speeds were 7.5°/sec, 15°/sec, 30°/sec and 60°/sec in clockwise and anti-clockwise directions.

From the duration of the after-sensations reported in Phase I the subjects were divided into two approximately matched groups, which in Phase II were given different instructions. The *control* group received the same *weak* instructions as employed in Phase I. They were told that this second test was to check the previous findings and that they should "press the button when you think that the sensation of turning has

THE EFFECT OF INSTRUCTIONS UPON POST-ROTATIONAL SENSATIONS AND NYSTAGMUS

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By the technique of sensation cupulometry two matched groups, each of 7 subjects, were obtained. In a subsequent test one group received "strong" instructions and the other, which served as a control, "weak" instructions similar to those employed in the initial test. With the "strong" instructions there was a prolongation ($p=0.001$) of the reported after-sensation and a fall ($p=0.02$) in threshold of the sensation cupulogram but no change in "slope". In the control group there was no significant change of "slope" or "threshold". The decay of post-rotational nystagmus was prolonged in the "strong" instruction group and reduced in the control group. It was inferred that the increase in the duration of the after-sensation was produced by a change in the afferent signal rather than by an alteration of sensory threshold.

INTRODUCTION

Recent studies (Holland 1961, Reason 1963) have demonstrated that following visual inspection of a rotating spiral the reported persistence of illusory motion of the spiral (spiral after-effect) was influenced by the strength or vehemence of the instructions given to the subjects. Under the same conditions of objective stimulation it was found that "high criterion" or *strong* instructions produced a significantly longer after-effect than did the "low criterion" or *weak* instructions.

The exponential decay (Taylor 1963) of the illusory motion makes it difficult for the subject to give an unambiguous judgement of the time at which the apparent motion is no longer perceptible, so that he is placed in a judgement situation where he is particularly susceptible to instruction effects (Biderman & Zimmer 1962). As the sensation of turning evoked by an impulsive angular stimulus also decays in an exponential manner (van Egmond, Groen & Jongkees, 1949) it was considered that in this analogous situation the duration of the reported after-sensation would also be influenced by instructions. Furthermore in the vestibular sensory system the ability to quantify nystagmus, which is perhaps more closely related to the afferent signal (Lorente de Nó 1933) than the sensation of turning, may provide a better understanding of the mechanism by which instructions exert their effect.

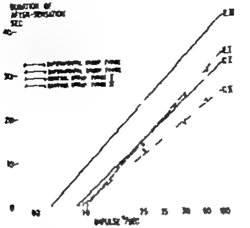

FIG. 1 Mean sensation cupulogram of the four experimental conditions. Each point is the erage of 14 observation from 7 subjects.

ubjects and between the after-sensation times at the four turntable speeds in both subject-groups and in each phase of the experiment. No effect ttributable to the direction of rotation was detected

Sens tion cupulogram

The regression equation relating log impulse to duration of sensation was calculated for each subject in each experimental phase From the regression equation the intercept at $t=0$ was calculated in order to deter mine the magnitude of the impulse corresponding to the "threshold" of the sensati n cupulogram, and the gradient of the line was used to calculate the time constant (Π/Δ) of the exponential function

In Phase I there was no significant difference in either "threshold or "slope between the *experimental* and *control* groups, thus the simple matching procedure, based on the total after sensation time, was justified

TABLE 1 *Mean total duration of after sensations for the four impulses and the ignificance of the differences according to group and phase*

	Duration of Sensation, sec		
	Phase (P)		Difference
	I	II	P_I-P_{II}
Experimental group (E)	81.53	121.48	−39.90 $p = 0.001$
Control group (C)	81.51	67.49	17.05 $p = 0.01$
Difference E-C	0.01 NS	56.99 p 0.001	

stopped. The *experimental* group were given *strong* instructions which involved telling them ... to be *absolutely sure* that the *sensation had* stopped before they pressed the button. The instructions were repeated and spoken with emphasis.

In Phase II each subject again experienced eight impulsive stimuli, the order of presentation being determined, as in Phase I, according to an incomplete Latin square design.

Subjects

Fourteen male subjects, who represented a fair cross section of Royal Air Force trade groups, participated in the experiment. None had prolonged flying experience nor had they prior experience of rotational tests of labyrinthine function. All were in normal health and without clinical evidence of aural disease. The median age of the group was 20 years, range 17–26 years.

The mean *E* score from the Maudsley Personality Inventory (MPI) was 30.5 and the mean N score 20.1. (Norms *E* = 24.6, N = 17.8 (Jensen 1958).)

RESULTS

Duration of Post Rotational Sensations

The effect of instructions on the duration of the reported after-sensation of turning is summarised in Fig. 1 in which the mean sensation times are plotted against the logarithm of turntable velocity in the form of a *sensation cupulogram* (van Egmond, Groen & Jongkees 1948). Statistical analysis of these subjective data has been carried out in two ways. Firstly by analysis of the total duration of the after-sensations reported by each subject in each phase of the experiment, and secondly by analysis of the "slope" and "threshold" values of the individual cupulograms.

Total after-sensation times

In Table 1 the mean durations of the after-sensations, produced by the eight impulses used in each test session, are assembled according to subject group and the phase of the experiment. As in Phase I the sum of the after-sensations reported by each subject was used to generate the *control* and *experimental* groups; the means for these two groups were similar while the variance of the reported after-sensation times was found not to differ significantly. However, in Phase II those subjects who received the *strong* instructions (*experimental* group) reported significantly (p = 0.001) longer after-sensations than the *control* group, who received the same *weak* instructions as in Phase I. In the *control* group the total after-sensations were shorter (p = 0.01) in Phase II than in Phase I.

Analysis of variance revealed significant (p = 0.001) differences between

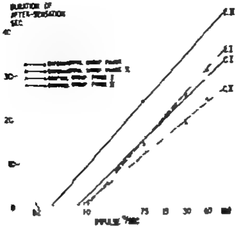

Fig. 1 Mean sensation cupulograms of the four experimental conditions. Each point is the average of 14 observations from 7 subjects.

subjects and between the after-sensation times at the four turntable speeds in both subject-groups and in each phase of the experiment. No effect attributable to the direction of rotation was detected.

Sensation cupulogram

The regression equation relating log impulse to duration of sensation was calculated for each subject in each experimental phase. From the regression equation the intercept at $t=0$ was calculated in order to determine the magnitude of the impulse corresponding to the "threshold" of the sensation cupulogram, and the gradient of the line was used to calculate the time constant (Π/Δ) of the exponential function.

In Phase I there was no significant difference in either "threshold" or "slope" between the *experimental* and *control* groups, thus the simple matching procedure, based on the total after-sensation time, was justified.

Table 1. *Mean total duration of after sensations for the four impulses and the significance of the differences according to group and phase*

	Duration of Sensation, sec		
	Phase (P)		Difference
	I	II	$P_I - P_{II}$
Experimental group (E)	84.58	124.48	−39.90 $p = 0.001$
Control group (C)	84.54	67.49	17.05 $p = 0.01$
Difference E−C	0.04 NS	56.99 $p = 0.001$	

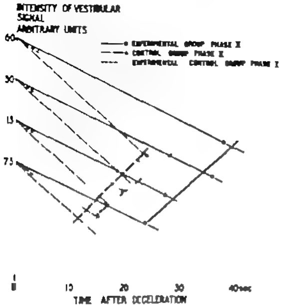

Fig 2

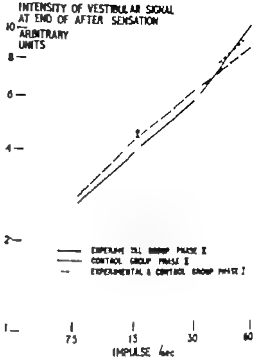

Fig 3

Fig. 2. Hypothetical mean sensation threshold derived from objective and subjective measures of vestibular activity.

Fig. 3. Relation of threshold to intensity of impulse. Values derived from Fig. 2.

The mean threshold was 0.7°/sec and the mean slope 7.8 sec; these values fall within the normal range of Hulk & Jongkees (1948) and close to the median values for a population distribution obtained in our laboratory (Benson, unpublished).

In Phase II *strong* instructions produced a displacement of the mean sensation cupulogram to the left. Whereas no significant change in the calculated "slope" occurred between Phase I and II, "threshold" was

TABLE 2. *Mean time constants of decay (in seconds) obtained from regression equations of angular velocity of post rotational nystagmus following impulsive stimuli of 60°/sec clockwise and anti-clockwise*

The bracketed figures are the mean calculated slopes of the sensation cupulograms.

	Phase I	Phase II	Difference $T_I - T_{II}$
Experimental group (E)	16.2 (8.8)	21.9 (7.[illegible])	−5.7 NS
Control group (C)	16.0 (6.8)	12.2 (5.7)	4.7 $p < 0.05$
Difference E–C	−0.7 NS	9.7 $p < 0.02$	

reduced from 1.04 /sec to 0.24 /sec, this difference being significant at the p = 0.02 level. In contrast there was an apparent reduction in the "slope" of the cupulogram of the *control* group but this was not supported by the analysis of the calculated "slope" values. Likewise no difference between the calculated threshold values in Phase I and II was demonstrated.

Post Rotational Nystagmus

Nystagmus was recorded for 30 sec following each impulsive stimulus. With the smaller stimuli measurable nystagmus was not obtained from all subjects, so analysis was restricted to that obtained following the 60 /sec impulses. The slope of the slow component of each nystagmic eye movement was measured and the angular velocity calculated. The regression of log angular velocity against time after deceleration was subsequently calculated for each subject in both Phase I and Phase II, the values fo rotation to right nd left being combined.

The mean values of the time constants (Π/Δ) which describe the decay of nystagmus were obtained from the gradients of the regression equations and are shown in Table 2. In Phase I the *control* and *experimental* groups were similar but in Phase II the mean value of Π/Δ rose in the *experimental* group and fell in the *control* group. The difference between the Π/Δ values in the *control* group in Phase I and II was significant at the $p = 0.0$ level (Wilcoxon Test) and between *control* and *experimental* groups in Phase II ($p = 0.02$, Mann & Whitney U Test). Non-parametric tests of significance were employed because of the non normal distribution of the calculated Π/Δ values.

As there is some evidence (Collins & Guedry 1962) that the magnitude of labyrinthine nystagmus, engendered by a particular stimulus, is related to the level of arousal the amplitude of nystagmus recorded during the first 3 sec after the 60 /sec impulse was measured. It was apparent from inspection of the figures that there was no significant difference between *experimental* and *control* groups nor between Phases I and II.

Skin Resistance

In an attempt to obtain an indicant of the subject level of arousal, skin resistance was determined before each impulsive stimulus as well as the magnitude of the maximum fall in resistance evoked by the stopping of the turntable (Preber 1958). However neither of these measures showed a significant difference between *experimental* and *control* groups in Phase I or in Phase II nor between Phases I and II.

Relation of Duration of After Sensation to Personality

Earlier experiments (Reason, 1963) had shown that there was a positive correlation between the effect of instruction on the reported duration of

the spiral after-effect and "extraversion" as measured by the Maudsley Personality Inventory

In the present experiment the rank order correlation (r) between the difference in the total duration of the post rotatory after sensation in Phases I and II in the *experimental* group and the "extraversion scale" score of the MPI was found to be +0.22 which was not significant

In the *control* group the difference between total after sensation times in Phases I and II represented a habituation effect in contrast to the instruction effect seen in the *experimental* group This difference was also found to give a positive but not significant rank order correlation of +0 46 with the "extraversion scale" score of the MPI

DISCUSSION

This experiment demonstrated unequivocally that the duration of the reported after sensation evoked by an impulsive angular stimulus was influenced by the instructions received by the subjects. As the decay of the sensation of turning is relatively slow in the "threshold" zone a small shift in the criterion which determines when the subject decides to indicate that the sensation has disappeared can be manifest as an appreciable increment in the duration of the reported after sensation In terms of the stimulus response relationship typified by the sensation cupulogram of van Egmond Groen & Jongkees (1948) the *strong* instruction produced a depression of the sensory "threshold" without a significant change in the "slope" of the cupulogram With repetition of the weak instruction there was no significant alteration of either "slope" or "threshold" though the mean slope was lower The latter is in accord with the observations of de Wit (1953) who demonstrated a similar reduction in the "slope" or "habituation" of the cupulogram with iteration of the test

On the evidence provided by the sensation cupulogram alone the effect of instruction is apparently without complication A *strong* instruction decreases the sensory threshold over that obtained with a *weak* instruction while repetition of the same *weak* instruction leaves threshold unchanged and allows habituation to occur However it has become apparent that the sensation cupulogram is not derived from the vestibular afferent signal in the relatively simple manner originally proposed by van Egmond Groen & Jongkees (1949) For if as was suggested the sensation threshold were a constant value then the time constant of decay (i e "slope") of the sensation cupulogram should correspond to the time constant of decay of the vestibular afferent signal as indicated by the decay of nystagmus slow phase velocity Subsequently several workers (van Egmond & Groen 1955 Stahle 1956 Groen 1957) drew attention to the disparity in the H I values obtained by sensation and nystagmus cupulometry while in a series of over 100 subjects examined in our laboratory it was found that the time constants of decay obtained by measurement of slow phase nystagmus

velocity following an impulsive stimulus were consistently larger than the H/Δ value obtained from the slope of the sensation cupulograms. This feature was also apparent in the present experiment (Table 2)

Hypothetically there are a number of different ways in which this disparity could arise If the sensory threshold were constant, then the time constant of decay of the afferent signal would have to increase as the magnitude of the stimulus decreased or alternatively the magnitude of the afferent signal following an impulse, would have to be related by a non linear function to the intensity of the stimulus These two hypothetical mechanisms are untenable not only because they are not in accord with the theory of the behaviour of the end-organ propounded by van Egmond, Groen & Jongkees (1949) but also because experimental measurement of the discharge of ampullary receptors (Groen Löwenstein & Vendrick, 19) and the study of post rotational nystagmus (Aschan, Bergstedt & Stahle, 1956 Stahle, 1957) have shown that the magnitude of the afferent signal, produced by an angular impulse, bore a linear relationship to the intensity of the stimulus, and that the time constant of decay is constant irrespective of the magnitude of the stimulus

It is thus more likely that the difference in time constants obtained by subjective and objective methods is to be explained by the variability of the sensation threshold Experimental evidence suggests that this threshold is not constant but varies with the intensity and duration of the preceding stimulus in common with the limen of other sensory modalities, it is adaptive (Hallpike & Hood, 1953) This concept is illustrated graphically in Fig 2. The ordinate represents the intensity of th vestibular afferent signal on a logarithmic scale The lines originating at the $g = 60$ 30 15 and 7.5 positions delineate the exponential decay of the afferent signal for each f the four impulses used in the present experiment, the gradient of each line being determined by the mean time constant of decay of nystag mu in each experimental condition. (Phase I values were combined in order t facilitat comparison between the effect of weak and strong instruction in Phase II) The position of the filled points on the graph was determined by the ordinate of the decay line appropriate to the impulse and experi mental condition, at the time at which the after sensation was reported to have disappeared.

From such a graphical representation it is apparent that the "threshold" fell progressively as the intensity of the impulsive stimulus was decreased. The relationship between these two variables is essentially linear as is shown in Fig 3. The surprising feature revealed by this analysis is that

1 (In this laboratory measurement [of] several individuals of the angular [ve]locity [o]f post rotational [n]ystagm[us] duri[n]g cupulometric tests ha[s] confirmed the observ[a]tions [o]f Asche[n] et al (1956) I[n] the majority of subject[s] H/Δ [v]alues were identical at all impulses between 10°/sec and 60 sec, though i[n a] minority nystagmus [v]elocity decayed more [ra]pidly with the smaller impulses. Individuals who beha[v]ed in this way charac teristically produced the curved cupulogram described by Hulk & Jongkees (1948)

the threshold values *for a particular impulse* lay close to one another and changed but little with the strength of the instruction. The threshold was apparently lowest in those subjects who received the *strong* instruction but this was not consistent at all impulse magnitudes and did not differ significantly from the values obtained in the other experimental conditions. Thus it may be tentatively concluded that the principal factor which underlay the alteration in the duration of the after-sensation was the change with instruction of the rate of decay of the afferent vestibular signal.

The demonstration of an alteration in the pattern of activity of the vestibulo-ocular reflex implies a change in the afferent vestibular signal but this may be mediated either peripherally or at higher neuronal levels within the vestibular afferent projection. It is most unlikely that the *dynamics of the canal–cupula–endolymph system can be regulated by* neuronal activity, though an alteration in the stimulus response relationship of the sensory cells *consequent to the activity of efferent neurones is,* by comparison with other end-organs, a possible mechanism which receives some support from the experiments of Schmidt (1962) and Sala (1965).

Modification of vestibular responses can also occur as the result of changes in the level of "behavioural arousal" (Collins & Guedry, 1962). Although in the present experiment measures of skin resistance and the amplitude of nystagmus provided no proof that "arousal" was enhanced in the *strong* instruction condition, it can be argued that the more demanding task situation achieved by the *strong* instruction would act in this manner while conversely, "arousal" would be lower in the *control* group in Phase II when the subjects performed a task with which they were already familiar. Heightened "arousal" *per se* should increase the angular velocity of post-rotational nystagmus but need not give rise to a change in the rate of decay. However, an apparent change in time constant would occur if, following the impulsive deceleration, arousal decayed more rapidly in the *control* than in the *experimental* group in Phase II.

The arguments so far adduced lead to the conclusion that instruction exerts its effect by increasing the neuronal signal rather than by alteration of sensory threshold, but caution must be exercised in equating measures derived from nystagmus with the neuronal signal in sensory projection. The discrepancy between the *H–t* values obtained from sensation and nystagmus cupulometry led Stahle (1958) to the conclusion that both the sensation of turning and nystagmus are influenced by extra-labyrinthine factors of differing nature. Although he considered that nystagmus recorded with the eyes closed reflected most closely the behaviour of the end-organ, Groen (1962) pointed out that the time constant of decay derived from nystagmus measures is still less than that predicted from the physical properties of *the canal–cupula–endolymph system.* He postulated that the "coupling" between the vestibular afferent signal at the periphery and the *neuronal* centres which control the efferent manifesta-

tions of vestibular activity is adaptive and that the strength of the inhibitory component of this coupling is greater for the sensation of turning than for nystagmus. This model therefore offers an alternative hypothesis in which instruction exerts its influence by alteration of the coupling between end-organ and neural centres This is an acceptable explanation of the changes observed in nystagmus time constant between Phases I and II but fails to account for the absence of a comparable increase in sl pe of the sensation cupulogram in the *strong* instruction condition unless a dissociation of the coupling between nystagmus and sensation is postulated for this experimental condition

Irrespective of the mechanisms by which instruction modifies post rotational vestibular responses these experiments have demonstrated further the lat lity of both the sensations and nystagmus engendered by stimulation of semi-circular canal receptors They also point to the necessity to standardize instructi n t subjects who undergo rotational tests of vestibular function, a part of eith r clinical or experimental investigation, especially when inter subject differences are to be assessed

ACKNOWLEDGMENTS

W wish t tha k Miss H M. Ferres for her help with statistical naly si and Mrs A. Coupe and Mrs M Perry for tech ical assista ce

ZUSAMMENFASSUNG

Unt Anwendung de Technik der Empfindu gs-Cupulom trie wurden zw i glei hartige Gruppen von Versu hspersonen unt rsucht. Bei Wiederh lung des Versuches gaben die V rsuchspersonen der Gruppe die eine ingehend Belehrung erhalten hatt langer nh liende V chempfi dungen an ($p = 0.001$) l die V suchspersonen der Gruppe die dieselbe kurz Belehrung erhalten hatte wie im Erst ersuch Die ingehend belehrte Gruppe wies inen Abfall der Rei schw lle ($p = 0.02$) af jedoch keine Änderung des Gef lles. In der K ntrollgruppe wurd k e ken lehnend Veränderung der Reizschwelle oder des Gef lles gefu den. Die Abnahm les Nachdreh-Nystagm s war verlängert i der ingehend belehrten Gruppe und verkürzt i der K ntrollgruppe E wurde a genommen d s die Zu hm der Dauer von Nach-Sensati en ber nut l And rung des ilieren len Sign ls ls mit ner Versch ebung der R izschw lle in Zusamm hang stand.

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BÉKÉSY AUDIOMETRY, SISI TEST AND CONTRALATERAL MASKING

Preliminary Report

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Preliminary investigations indicate that contralateral masking exerts a significant influence on auditory diagnostic procedures in which a sustained stimulation is involved. In Békésy tracings, masking caused separation between curves for interrupted and continuous tones and reduction of tracing width of the latter. In the SISI-test the scores improved at higher frequencies. In patients with VIIIth nerve lesion excessive temporary threshold shifts appeared when the unaffected ear was stimulated with continuous white noise.

In recent years Békésy audiometry by the method of Jerger (Jerger 1960) and the SISI test (Jerger, Shedd & Harford, 1959) have become standard procedures in the examination of patients with unilateral perceptive hearing loss in order to determine the site of lesion. In most cases—dependent upon the degree of loss—the exclusion of the better ear necessitates the use of a masker. Even minor alterations in test conditions may cause significant changes in the outcome of auditory tests and the routine application of making noise to the non-test ear during the named procedures warrants further study. With the use of insert-receivers instead of the customary supra-aural headphones it is possible to increase the transcranial attenuation. Cross conduction of the test signal can now often be obviated, even when no masking is used, and a considerable amount of masking can be applied without any risk of overmasking. When indicated, the pericranial attenuation can be increased by covering the normal ear with a circum-aural noise defender which was modified to reduce the occlusion effect and to increase the sound damping properties. By these means it is possible to test most patients without masking and to evaluate the effects of a masker.

PROCEDURE

All acoustic stimuli were delivered by insert receivers, the characteristics of which will be furnished in a later publication. The phones were 10-ohm Beyer DT 307 of the hearing aid type.

This work was supported by a grant from Statens Almindelige Videnskabsfond.

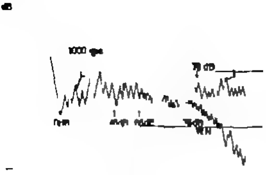


FIG. 1

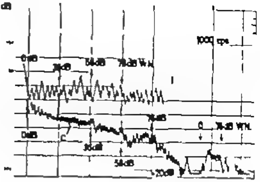


FIG. 2

FIG. 1 Fixed frequency tracings with increasing contralateral masking in a 61 year-old female with a right acoustic neuroma Numerals indicate the amount of masking Arrows indicate the moments when the intensity of the masker was changed Tracings obtained without masking showed threshold curves for C (continuous tone) and I (interrupted tone) to be superimposed

FIG. 2 Fixed frequency tracings in a 48-year-old female with a left acoustic neuroma For explanation of numerals see 1 →+20 dB indicates an increase in the intensity of the test tone at this moment

Békésy audiometry was carried out with a Grason Stadler E-800 audiometer attenuation rate was always slow" (2.5 dB per second) Sweep-frequency tracings for interrupted (I) and for continuous (C) tones were recorded without masking and later with a continuous white noise at an intensity of 76 dB in the unaffected ear The noise level was measured in the 2 cc coupler of the Brüel & Kjær model 2203 sound level meter linear curve Fixed frequency recordings for I and C were made at no less than 3 frequencies first without and then with increasing contralateral masking

The SISI equipment which has been described previously (Blegvad 1966) is connected to a Madsen OB 60 pure tone audiometer The testing was done 20 dB above threshold (as determined without masking) at 3 or more frequencies with series of increments ranging from 0.5–5 dB the intensity variations being of constant magnitude within each series Test runs without and with 80 dB masking were conducted alternately until—if possible—psychometric functions were obtained for both conditions

For masking the unfiltered thermal noise generated by the respective audiometers was used

RESULTS

Results are reported from the first seven patients with unilateral perceptive deafness examined by this method The findings should be considered as preliminary and only the most striking features are mentioned

In 3 patients suffering from a tumor of the VIIIth nerve the Békésy tracings for continuous tone were found to be significantly influenced by contralateral masking In the first patient a marked drift in threshold

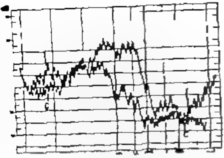
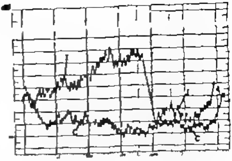


Fig. 3 a.



F 3 b.

Fig. 3 a. S eep-frequency tracings in 28-yea -old f mal with l ft acoustic neuroma (as yet not surgically confirmed) N masking was used.

Fig. 3 b. S eep-frequency tracings in the same patient as they ppeared when 76 dB contin ous white noise was pplied t the unaffected ea d ring the examination.

could be induced at frequencies where otherwise no shift occurred (Fig 1) In all 3 patients the temporary threshold shifts could be augmented (Fig. 2) and frequently a reduction in tracking amplitude was noted. The changes were reflected in sweep-frequency curves (Fig 3) as well as in the fixed-frequency recordings.

When SISI testing according to the outlined procedure was attempted in the first patient, it was found to be impracticable at 4000 cps because of tone-decay At 1000 and 250 cps, testing could be carried through when no masking was applied to the opposite ear scores were low but for 3.5 and 4 dB increments respectively she responded quite consistently With 80 dB masking the test became impossible also at these frequencies, because of rapid loss of perception of both tone and pips. For this reason a stepwise introduction of the noise was undertaken. With 40–50 dB masking, responses became scattered and at a level of 50–55 dB she stopped completely after the lapse of 15–20 seconds When the noise was switched off she started responding regularly again When masking was resumed, she gave up once more after approximately 20 seconds. This course of events could be repeated several times.

In a patient with a 6-month history of progressive loss, Békésy tracings obtained without masking showed C and I recordings to be superimposed in the 125 to 1200 cps range and only slightly separated at higher frequencies (Fig 4 *a*) When the xamination was repeated with 76 dB con tralateral masking the result was clearly different, the amplitude of the C tracing being noticeably reduced and the mid-points of curves separated even at lower frequencies (Fig 4 *b*) In fixed-frequency tracings corre sponding hanges were seen. The initial definite impression of a cochlear type lesion th became less certain. In the SISI testing of this patient, the most conspicuous finding was the *improvement* of scores at 4 kc when ma ki g was applied For 1 dB intensity variations for example scores were repeatedly questionable (20–55%) when no masking was used,

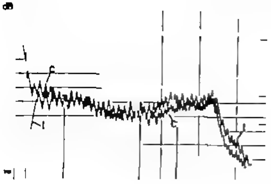


Fig. 4 a

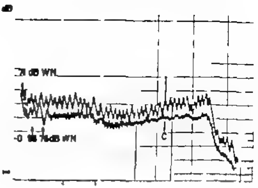


Fig. 4 b

Fig. 4 a. Sweep-frequency tracing in a 62-year-old female with right-sided sensori-neural loss, cause yet unknown. No masking.

Fig. 4 b. Sweep-frequency tracing in the same patient. 76 dB white noise was applied continuously to the opposite ear during the I recording. For irrelevant reasons the masking was introduced in steps when the C recording was made.

whereas scores of 90–100% were obtained when the opposite ear was stimulated by 80 dB white noise.

In a patient who experienced sudden loss 9 months prior to the examination, masking produced quite similar alterations: 8–12 dB separation between curves in the whole frequency range, reduction of amplitude and increase in SISI scores at higher frequencies. The loss was of the flat type at a level around 60 dB.

In another patient with loss of sudden onset (duration 3 weeks), Békésy audiometry for pulsed tones revealed a pronounced high frequency loss. Hearing was essentially normal in the 125–1700 cps range; from this point the curve dropped abruptly reaching the 85 dB level at 4000 cps. The I tracings were not affected by contralateral masking, whereas the continuous tone tracings at the damaged frequencies were influenced in the same manner as in the tumor cases (Figs. 5 a and 5 b). In the SISI test masking caused a marked increase in scores for 1000 and 1500 cps (e.g. 1000 cps, 1 dB increments: 0% → 70%). At 2000 cps the score was 0 %, even for 5 dB increments, irrespective of the masking condition.

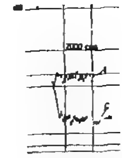
It should be mentioned that in normal listeners we found a similar significant improvement in the ability to detect small intensity variations with the use of continuous contralateral masker (to be published).

Finally, in a patient with a 6-year-old history of Lermoyez Disease Békésy audiometry and SISI tests were literally unaffected by masking.

DISCUSSION

The present results were selected with particular consideration of the pure tone audiograms and the interaural attenuation for our insert receivers (which was determined previously in subjects with complete unilateral deafness).

F a. 5 a.



F 5 b

FIG. 5 a. Fixed-frequency traci gs i 44-year-old mal who dev loped sudden high frequency loss 3 weeks before the examinations. Increasi g contralateral masking Explanation as for 1 and 2.

FIG. 5 b Tracings obtained without masking i th same patient. Duri g the testi g the good ear was covered by noise excludi g cap t improv perfora tal tt nation.

This *per se* should eliminate the possibility that the changes observed were due to physical transmission of the masking noise to the test ear The fact that thresholds for interrupted tones remained essentially un affected, strongly supports the view that overmasking did not occur

Cross conduction of the test stimulus to the unaffected ear can also be excluded except in patients with pronounced perstimulatory threshold shifts. As the threshold deteriorates, the demand for masking increases. If masking is insufficient, a one-to-one relationship between the increase in the intensity of the masker and the shift in threshold is to be expected. This does not appear to be the case.

The possibility that middle-ear muscle activity evoked by the noise could play a part, ought to be touched upon Contraction of the middle-ear muscles will change the threshold for frequencies below the resonance point of the middle-ear and both C and I tracings should be affected in the same way The contraction occurs with a very short period of latency and t nds to decrease over time. These facts do not fit with our findings. The explanation will hav to be sought at other levels in the hearing mechanism.

Brunetti (1961) by th method of Carhart (1937) examined the central auditory dapti n In a majority of normal hearing subjects the adaption could be accel rated through the introduction f 30 dB thermal noise in the contralateral ea In 20% of the subjects a deceleration was found In patient with variou CNS lesions studied with this procedure, alterations n dapti n were noted too, but the paper contains no quantitative informa-t n

In p tient with neuroma of the Jugular foramen, Harbert & Young (1964) observed a marked drift of threshold in the Békésy fixed-frequency C curve The drift was not seen unless the opposite ear was masked (100 dB whit n ise) They ascribed the phenomenon to overmasking

Dirks & Malmquist (1965) using *Békésy fixed frequency* technique studied shifts in air-conduction thresholds for pulsed and constant pure tones produced by continuous contralateral masking (a narrow band masker centered around 4000 cps) The greater shifts occurred at 4000 cps. With 70 dB masking the mean change for pulsed tracing was 0 91 dB and for continuous 6 06 dB viz the alterations tend to separate the tracings. Furthermore, the excursions in the latter tracing were found to diminish by 30% on the average Only normal hearing subjects were investigated, and the authors do not mention the possible implications of their findings for the current diagnostic use of Békésy audiometry which is based on a comparison of thresholds for constant and intermittant tones. Clinical importance has also been attached to measurement of the threshold excur sions. It is interesting that also this parameter will often depend upon the degree of masking delivered to the contralateral ear

The general accepted indications for use of a masker are such that the masking effects described may play a major role in clinical audiological procedures that involve perstimulatory examinations

ZUSAMMENFASSUNG

Vorläufige Untersuchungen zeigen dass kontralaterale Maskierung einen signifikanten Einfluss auf audiologisch-diagnostische Verfahren in welche eine dauerhafte Stimulation eingeht ausübt Bei den Békésy kurven verursachte die Maskierung eine Sonderung zwischen den *Zeichen von pulsierenden und stetigen* Tönen und verminderte die Ausschläge der stetigen Tonzeichen In der SISI Probe wurden die Scores der höheren Frequenzen verbessert Bei Patienten mit Beschädigung des VIII Gehirnnervs entstanden exzessive zeitweilige Schwellen Änderungen wenn das nichtbefallene Ohr mit kontinuierlichem weissem Geräusch stimuliert wurde

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RECONSTRUCTIVE MICRO-SURGERY OF THE EARDRUM BY MEANS OF A TYMPANIC MEMBRANE HOMOGRAFT

Preliminary Report

J MARQUET
Antwerp Belgium

From th Institut Bunge A twerp

Different materials were recommended for reconstructive operations of the tympanic membran The author presents a new myringoplasty technique by usi g human graft kept under refrigeration in a preserv ing solution. These tympa ic membranes were taken from corpses. This technique produced not only ex ellent perative results, but must also be oted for th anatomical and physiological quality of the tympanic membranes reconstituted in this manner In addition the constitution of a tympani membrane bank i also an advantage it eliminates the taking of the graft during the operation itself

Since Wullstein and Zöllner opened the way in 1952 to tympanoplasty numbers of various surgical methods have been suggested. As this paper concerns especially a new material used to reconstruct the tympanic membrane we shall not reopen the discussion here concerning these various surgical methods. As to the choice of material to be used, it has also been the object of numerous publications

Thus, aft r having used total or partial skin grafts, pediculated or not, amniotic membrane, mucosa, periosteum, dura-mater vein, fascia-lata or f scia-temporalis graft and even cornea were suggested in succession

Several mixed techniques were described, where combined use of these materials was made Our aim is not to make a critical study of the use of these different techniques such an bsolutely objective study would be practically impossible as in addition to the problem of the material used, the kill with which the urgeon performs the operation represents a factor that is too v riable Nevertheless, in general it appears to be certain that most f the materials used up to date in competent hands have yielded most valuable results.

Certain materials used have of course undeniable advantages over others. Cert in techniques are predominant because they are easier others be cause of stronger neotympanums and others finally because they obtain a higher quality of phy iological results. None of these techniques, however and they includ the best, can claim to obtain an entire restoration of

the eardrum either in its *anatomical structure* or in its different physiological parameters

What material other than an intact tympanic membrane taken from a fresh corpse could give us the hope of getting so near to this ideal restoration?

It is this main idea that was the basis of our studies and that helped us to perform a myringoplasty of an absolutely new type that has to our knowledge as yet never been published

The use of human grafts required a complete adjustment of the problem of how to take the specimen and how to preserve it These problems will be discussed at length in a later paper but let us already say that the tympanic membrane bank that we have organized comprises eardrums taken *by binocular microscope on fresh corpses (less than 12 hours following death)* These tympanic membranes are then immediately disepithelialized and preserved in a solution at 1 to 5000 of the sodium salt of 2 (ethylmercurimercapto) benzoxazole-5 carboxylic acid (Cialit) at a temperature of ± 3

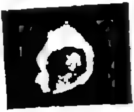
Criterions *that* determined the choice of this manner of preservation were for us essentially the guarantee of sterile and almost indefinite preservation of the graft and the extreme ease with which it is carried out (Fig 1)

TECHNIQUE

The case that we have chosen to carry out as the first essay of this new technique was a case carefully selected of a Wullstein type I a small boy of 8 years old whose ossicular function was intact whose tubar function was unimpaired and whose transmission deafness was caused essentially by a large perforation of the tympanic membrane This case was a great success which surpassed all our hopes (Fig 2) The operation was performed with a binocular microscope by transmeatal approach at a magnification of 25

After having removed by means of a micro-hook the cicatricious fibrous ligament circling the perforation and after quickening the extremity of the handle *of the malleus*, we loosened with the help of a curved micro-spatula the epithelial layer from the fibrous layer of the tympanic membrane remnants This loosening was performed from the inside towards the outside The loosened epithelium was handled with the utmost care so as to prevent it from being damaged Only three radiated incisions were made so as to be able *to* reflect it back against the edges of the external meatus At the same time two small calcification spots were very carefully loosened and removed

The tympanic graft that had *been* taken 4 weeks earlier was *taken out* of its preserving solution and thoroughly washed in a tepid physiological serum It was *then* applied on the edges of the perforation During this



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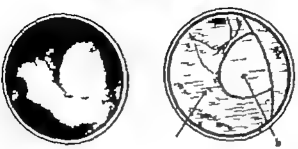

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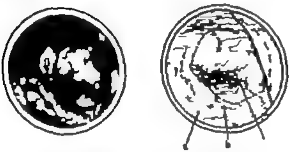

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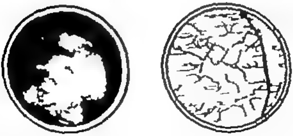

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FIG. 1 Drum graft ready for se

FIG. 2. Anterior margi al perforation of the eardrum. *a*, Drum remnant; *b*, drum per foration.

FIG. 3. Drum graft in place t the end of the intervention. *a*, Drum remnant; *b* graft covered by epitheli m; drum graft.

FIG. 4 Drum seen immediately after removal f the packi g *a*, The limit f the grafted zone i lmost no longer i ible

Fi Four weeks fter intervention the ascular invasion i complet

operation we were extremely surprised to see the ease with which the graft because of its natural conical shape and its own structure found its place immediately exactly as if it were a tympanic membrane put back into place after a stapedectomy There was no need in this case to fear that the graft would slip out of its place

Immediately after the tympanic membrane had been put into place the epithelium flap *that had temporarily been reflected against the edges* of the external canal was applied to the graft and carefully spread over it At that moment the tympanic membrane presented a practically normal aspect (Fig 3) A few pieces of synthetic sponge were placed all around the perforation so as to exert a slight even and continuous pressure

It is to be noted that we used no means of support in the tympanic cavity such as gelfoam in order to hasten the healing and mainly so because the graft adheres so perfectly to the edges of the perforation that no element of support is necessary Three days later the synthetic sponge packing was removed At this moment the tympanic membrane had exactly the same aspect as that of an eardrum when the packing is removed after stapedectomy (Fig 4)

The postoperative course was normal and there was an immediate improvement in hearing Two weeks after the operation we proceeded to tidy up the eardrum After having removed a thin limpid and transparent crust the tympanic membrane appeared and was practically normal Only a very fine pink edging and a slight pearly colouring of the graft could be noticed and makes one suspect that a perforation had existed (Fig 5)

At high power magnification one could see that peripheral blood vessels had completely invaded the graft all round the tympanic membrane and *mainly at its antero-inferior edge* (This little patient was seen regularly)

Whereas the audiometric examination indicated a complete hearing recovery after 2 months it is impossible at otoscopic examination to define *the exact limits of the graft The tympanic membrane is perfectly* adherent to the handle of the malleus and is entirely mobile with Siegel's speculum

Since the first operation was performed having thus consisted in transplanting to a *small boy aged 8 a tympanic membrane taken from a* 48-year old woman and preserved during 4 weeks, we have performed this same operation several times in different cases of various types of marginal perforations, *and also of completely destroyed tympanic membranes*

So far we have limited ourselves to using only the conjunctive wefts of the tympanic membrane These having previously been disepithelialized and the annular ligament *removed all around the tympanic membrane* during the preparation of the graft The size of the grafts thus obtained necessarily limits the use of this technique to perforations smaller than that of the graft So it is *important to have a choice of* various sized tympanic grafts

We have reported only the cases with at least 3 months follow up (October 1965 until May 1966) *Of these 17 cases* whose ages vary between 8

and 67 we have only one complete failure and one partial failure to deplore the partial failure being retrieved later

It is also important to note that we have not taken into consideration the age or the sex of the donor The experiment seems indeed to indicate that these two factors would be of secondary importance and would hardly have any direct influence on the success of the operation

RESULTS

Group	Success	Failure	Partial failure
I *Perforations of less than 4 mm*			
Intact ossicular function. Dry middle ear for at least 6 months.			
Infectious etiology	cases	—	—
Etiology through burn by half-burnt l ders	1 case	—	—
II. *Large central perf rati ns large than 4 mm*			
Infectious etiology			
I tact ossicula function Middle ea dry for at least 6 month	2 cases	—	—
Intact ossicula function Middle ea dry onl in ppearance During th operation a widespread whit oed ma of th tympanic ca ity mucosa and of the tympanic membrane remn ts were observed Early failure This operat on was ttempted twice but with n result		1 case	
III *Post ri marginal perforati ns*			
I fections et logy Os icular f nction intact. Middle ea dry for at least 6 month	4 cases	—	—
Cholesteat matou eti logy Os icular function i tact M ddl ea dry for t least 6 months	2 cases	—	—
IV *A t ri marginal perf rati ns*			
I fections tiology Ossicular function intact Middle ea dry for t least 6 months	3 cases	—	—
V *Myringosl ped perg*			
Performed on an ld posterior margin l perforation of cholesteat matou origin. Middle ear dry I cus destroyed. Normal mobile st pes	1 case	—	—
Performed on an ld mast idectomy cavity Extremely large central perforation Attempt of a type III W llstein tympanoplasty P rtial f ilure W thin the first ten day small central perforation ppe red in the eotympanum. This same perforation was successf lly losed 2 months later also by homograft			1 case

It is still too soon to be able to predict the future of this technique in *tympanoplasty and to be able to forecast its extension to more complex* surgical techniques that necessitate the use of a larger graft which could be called a tympanomeatal homograft

We can ascertain here and now that the use of homograft tympanic membrane in micro-surgical reconstruction of the eardrum is a practice that enables us to forecast a widespread future

Nevertheless, these first cases operated on according to this technique allow us to ascertain that the implantation of human tympanic membranes is perfectly possible and that the eardrum thus transplanted after more or less long preservation in a preserving liquid at +3 has little or no risk of being eliminated, but that on the contrary this material must be considered as a choice material in myringoplasty The graft's morphological structure is in itself a quality that seems essential to us and that facilitates the surgical act

We wanted to present these first original cases of transplantation of a human eardrum keeping a more detailed and thorough study for a later paper

RESUMÉ

Différents matériaux furent préconisés pour les interventions reconstructives du *tympan L auteur présente une nouvelle technique de myringoplastie* utilisant des homogreffes de tympans conservés en frigo dans une solution de conservation Ces tympans sont prélevés sur des cadavres frais. Non seulement cette technique s est avérée donner d excellents résultats opératoires mais semble devoir être retenue pour la *qualité anatomique* et *physiologique des tympans ainsi* reconstitués La constitution d une banque de tympans presente en outre l avantage d éviter le prélèvement du greffon durant l intervention

ZUSAMMENFASSUNG

Verschiedene Materiale wurden für die wiederherstellenden Eingriffe des Trommelfelles empfohlen Der Verfasser beschreibt eine neue Technik der Myringoplastik, die darin besteht Trommelfelle zu verpflanzen diese wurden durch Tiefkühlung in einer Konservierungslösung aufbewahrt und sind frischen Leichnamen entnommen worden Diese Technik ergab nicht nur ausgezeichnete operative Resultate sondern ist auch bemerkenswert fur die anatomische und physiologische Natur der so wiederhergestellten Trommelfelle Die Errichtung einer Trommelfellbank stellt auch einen Vorteil dar denn es wird nicht langer nötig sein die Gewebe während des Eingriffes zu verpflanzen

La[illegible] Le m[illegible] 39
Antwerp, Belgium

THE DYNAMIC DC POTENTIAL IN THE COCHLEA OF THE GUINEA PIG (SUMMATING POTENTIAL)

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State University of Utrecht*

Using non polarising electrodes, changes of the DC potential in the various turns of the guinea pig's cochlea were measured during the application of sound stimuli by varying the parameters frequency, intensity and duration. In all turns of the cochlea a distinct change in polarity of the SP was found when the frequency of the stimulus was varied by a specific amount. The maximum of the +SP corresponds with the tonotopic projection of the experiments of von Békésy. The −SP is found in that part of the cochlea, which is in rest during the application of the sound stimulus. It is argued that the +SP and the −SP are generated in different parts of the organ of Corti. It is found that the latency of the −SP equals the latency of the AP. The +SP starts simultaneously with the CM and has no latency. The explanation is offered that the −SP can be considered as the summated effects of the asynchronous action potentials. The +SP can be considered as the consequence of a leakage current through the organ of Corti in accordance with Davis' supposition, concerning the mechanical sensorial transfer during the movement of the cochlear fluid. This leakage results in the generation of the +SP.

SYMBOLS

AP (Action Potential): summation of the elementary potentials of the nervus octavus, measured in the cochlea lymph.

CM (Cochlear Microphonics): AC potential equal in a certain amount to the sound stimulation of the cochlea and measured in the lymph.

SP (Summating Potential): dynamic DC potential measured in the cochlea during sound stimulation.

+SP (Positive Summating Potential): positive DC potential measured between the scala tympani and the neck muscles in that part of the cochlear partition which is moving during sound stimulation.

−SP (Negative Summating Potential): negative DC potential measured between scala tympani and neck muscles in that part of the cochlea which is in rest during sound stimulation.

Pure +SP: hypothetically found positive DC potential by subtracting the value of the −SP from the value of the +SP.

dB: sound pressure on the international standard of 2^{-4} dyne cm

INTRODUCTION

With the Summating Potential (SP) Davis Fernández & McAuliffe (1950) added a third cochlear potential to the well known Action Potential (AP) and Cochlear Microphonics (CM) Several papers on this subject have been published subsequently but the generator place of the SP still remains unknown In their first publication the authors attributed the SP to an active generating process in the organ of Corti the SP as they measured it in the scala media, appeared to be negative Goldstein (1954) was the first to describe a positive SP By Goldstein three types of the SP were presumed namely a strong positive SP a strong negative SP and a weak positive SP The strong negative SP was assumed to be of neural origin The generation of the negative and both positive SP s seemed to be influenced by the frequency of the delivered sound stimulus. No clear relation could be found at that moment

In 1958 Davis, Deatherage & Smith published the results of a research concerning the generator place of the positive and negative SP Although Davis in 1957 had stated that the generator place of the negative SP was situated in the outer haircells, he now claimed that the inner haircells should be held responsible for the negative SP and the outer haircells for the positive SP and CM This presumption was made based on experiments on the anoxaemic cavia cochlea whereas the formerly mentioned *experiments showed that the negative SP survived the anoxaemic state* of the cochlea better than the positive did The results of these experiments were in contradiction with von Békésy s view who deduced from vital staining experiments that the inner haircells are most vulnerable to oxygen lack

Goldstein observed that the SP under some conditions changed its polarity The change of polarity of the SP was most often attributed to the intensity of the stimulus and the pathological alterations of the cochlea although an influence of the frequency of the stimulus on the polarity of the SP was noted

A publication of *Konishi & Yasuno (1963) described an investigation* concerning the presence of the positive and negative SP in the various windings of the cavia cochlea A strict relationship between the frequency of the stimulus and the polarity of the SP could not be found

Problem

In his publications Davis *et al* (1950 1957) has pointed out that the generation of the SP should be a local phenomenon in the cochlea Presuming that the SP is formed during the occurrence of shearing forces between the ciliae of the haircells and the membrana tectoria (Davis) alterations of the SP are to be expected *qua* polarity and intensity in that part of the

cochlear partition which is moving during sound stimulation. If this were true, the SP should comport itself according to the place principle (von Békésy).

von Békésy's presentation of maximum movements along the cochlear partition should be a good guide in finding the maximum displacement of the basilar membrane of the cavia cochlea. With the scheme in mind it is possible to predict at any locus of electrode-placement the actual movement of the basilar membrane underneath the tip of the electrode, as a function of frequency.

In this paper experiments will be described in which the SP has been measured in different parts of the cochlea; from the results an explanation of the nature of the positive and negative SP is derived.

Methods

The experiments were carried out on 33 guinea pigs of an average weight of 350 grams. The animals were anaesthetised with Eunarcon,[1] a barbiturate in a dose of 60 mg/kg bodyweight, injected intraperitoneally after an introduction with atropine 0.02 mg/kg bodyweight. A tracheotomy was performed to allow artificial respiration in cases of emergency. The narcosis was held as light as possible to avoid any central depression of the cochlear function.

Surgical Procedure

The bulla tympanica was, as is usually, exposed by an approach from the ventro-lateral side, removing the salivary glands, proc. styloideus and the m. biventer. The bony wall of the bulla tympanica was removed with a dental drill. Afterwards, using a specially made directly driven burr with a diameter of approximately 80 μ holes were made in the scala tympani and vestibuli of the several windings of the cochlea.

Recording Procedure

The electrodes, employed for recording the negative and positive SP in the several windings of the cochlea, were made of silver with a mantle of silverchloride with an overall diameter of [illegible] μ. The reference electrode consisted of a silver-silverchloride plate and was placed between the neck muscles of the animal. In DC measurements, such as exploring the SP, it is very desirable to use silver/silverchloride electrodes in order to avoid any polarisation. In Fig. 1 a block signal is detected in saline solution to illustrate the possibility of polarisation. All electrodes other than the AgCl one give rise to differentiation of the input signal.

The signal derived from the animal was fed into a preamplifier (Tek

[1] Registered trade-mark.

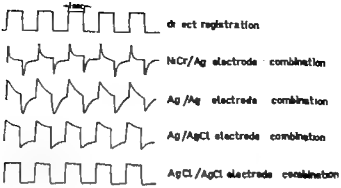

FIG. 1 The different electrode-combinations were compared. It wa found that the AgCl/AgCl electrode combination gave the best representation of the offered block pulse polarisation is hardly visible.

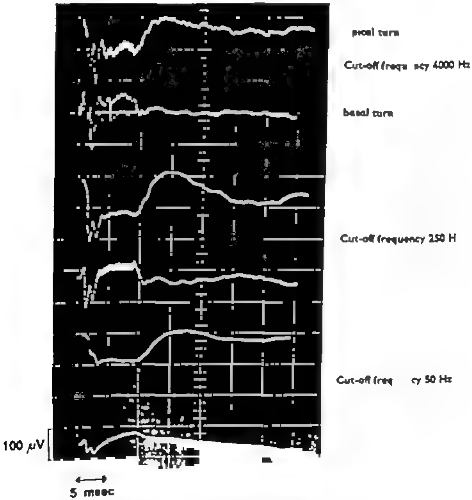

FIG. 2. Influence of th used filters (6 dB Oct) n th − SP d + SP regi trati n l sed frequency of th soundstimulus 1 4000 Hz I th basal turn the − SP leel found, the − SP is present in the pic l turn I th l w t part f th reg t ti with cut ff frequency of 50 Hz the l t ncy of th − SP is lea l d m strated the lack f the latency of the + SP is also vi ible It i sh wn th t the + SP st rted mmedi t ly t th beginning of the sound timulu The N1 d N2 dips re maller i th + SP regi tr tion than in the − SP because f the mi i g f th p re + SP nd th SP

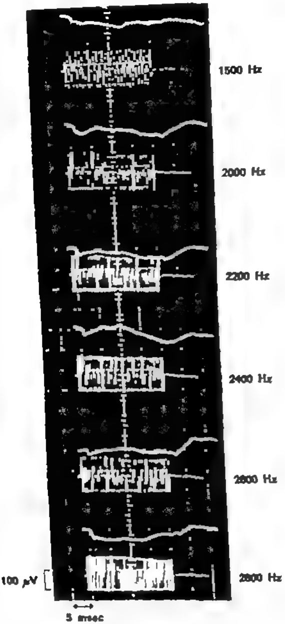

Fig. 2. Alteri g the +SP t the −SP by increasi g the frequency from 1500 Hz t 2800 H measured the third turn of the cochlea of the gui pig. The maximum alue f the SP w reached t frequency f the tim lus of 2400 Hz. At 2600 Hz the −SP i found ed it lue remained constant fter increasi g the frequency of the timulus.

t only no. 370) of which th l w frequency range was extended from 0.2 to 0.02 Hz. With a hort ignal (under 1 sec) little or no distortion of the ignal w seen on the oscilloscope Thi method produced a steady base-line on the oscill scope track, ince slow DC potentials, such as muscle

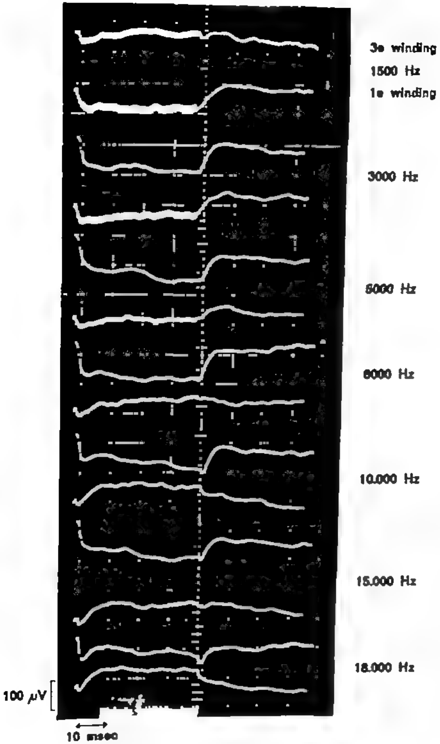

Fig. 4 +SP and −SP me ured in tl th rd d basal t n f th l l t sev ral frequencies of the soundstimulu In th t1 ird t rn the +SP t 1500 H lisappe red d is altered in a −SP at 3000 Hz that rem i ed con ta t through t th highe fre- quencies. In th basal winding a −SP i pres t t timul freq f 1500 H by increasing the frequency a +SP is formed w th a m imal in at 18,000 H

potentials, do not upset the amplifier. The CM was filtered out by a 6 dB/oct. low pass filter (cut-off frequency 50 Hz).

Sound Stimulus

The signal used consisted of rectangular tone bursts of 0.1–100 msec duration. Variable parameters were intensity and frequency. This signal was led to a telephone receiver of the condenser type, with a flat response from 300–30,000 Hz. The small size of the telephone receiver made it possible to introduce it into the external ear canal of the animal, close to the eardrum. The same electrical signal was fed into an identical telephone receiver which was attached to a 0.5 ml air coupler terminated by a calibrated condenser microphone imitating the external ear canal of the animal. The frequency characteristic of the condenser telephone was of such a high quality that it permitted even a true fidelity reproduction in air of an electrical signal of a single sinusoid (between 300 and 10 000 Hz). The intensity of the signal used during these experiments was always below distortion level (as observed on the oscilloscope screen, where its CM was displayed). It appeared that a maximum intensity level of approximately 80 dB could be maintained throughout the experiments at all frequencies. The lowest intensity level which could be used was approximately 35 dB. The intensity range over which the phenomena to be described below could be observed, was around 40 dB.

RESULTS

Shape and Occurrence of the SP

The first experiments were done in the third turn of the cochlea with a stimulus frequency in the range of 300–3000 Hz and a duration of 50 msec. In this case the signal had a maximum intensity of 70 dB to avoid any distortion of the middle and inner ear. The eventual distortion was controlled by watching the shape of the CM, derived from the third turn. When no distortion was present, the observation of the SP was started by switching on the low pass filter. Inspection of the SP was made easy. The −SP which was found under these conditions, started with a negative dip. It seemed, after switching on the low pass filter, that the negative dip was congruent with the usual N1 and N2 of the AP, when using the low pass filter to exclude the otherwise disturbing CM, the −SP had a latency of the same duration as the AP. At the end of the −SP a second negative dip was seen. It came at the same place as the off phenomenon and it had the same latency as the AP. Between the two negative dips at the start and the end of the −SP the signal remained negative. As for the +SP it is typical that its shape also started with a

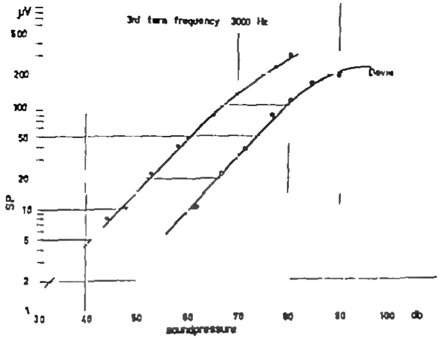

Fig 5 Input–output relation of the −SP by a frequency of the sound stimulus of 3000 Hz. By this frequency a −SP was present in the third turn. Our own measurements were compared with those of Davis *et al* (1958)

negative dip but subsequently it turned positive while at its end a slight negative dip was often found

In agreement with some other authors, we observed several forms in between the +SP and the −SP The midpart of the signal could even be zero Striking was the fact that the shapes of the −SP and the +SP were completely different By looking closely at the shape of the +SP and its transition into a −SP as a function of frequency it could be observed that this +SP must be a mixture of a far greater positive voltage and a constant negative voltage

The curve at the bottom of Fig 2 shows that the beginning has a slope upwards (positive) followed by a negative dip (N1 and N2) After this part the curve rises slowly to become positive again The negative part is here smaller than in the curve presented above the former because of the positive contribution The negative part clearly demonstrates a latency attributed to the formation of the N1 The +SP however shows no latency starts together with the CM and by this it reveals its presence already in the beginning of the recording

There is every reason to presume that the +SP found in the measurements is a mixture of a pure +SP and the −SP and has to be corrected for this negative amount This statement will be elucidated in the chapter on discussion

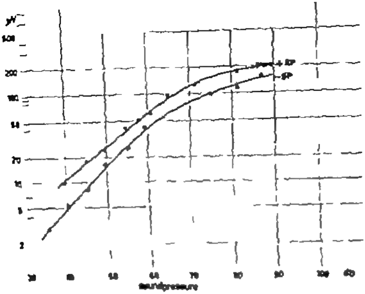

FIG. 6. Input-output relation of the "pure +SP" measured in the third turn of the cochlea. With a frequency of 1800 Hz a maximum value of the +SP was found. The value of the -SP was measured at a frequency of 4000 Hz.

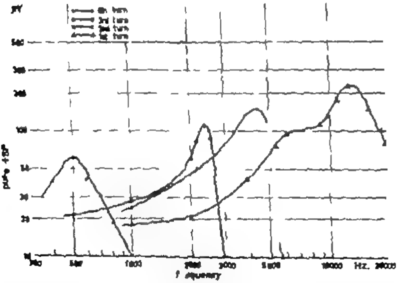

FIG. 7. Maximum values of the "pure +SP" found in the four turns of the cochlea of the guinea pig. The value of the -SP was measured at a soundpressure of 80 dB (about 110 V). The increasing of the maximum value of the "pure +SP" from the fourth turn to the basal turn could be the result of the change of the electrical resistance of the basilar membrane according to the work of Misrahy and co-workers (19-4).

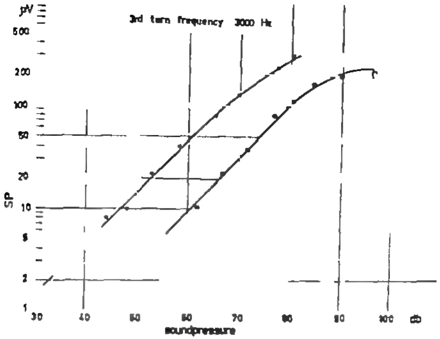

FIG 5 Input–output relati n of the −SP by a frequency of the soundstimulu of 3000 Hz. By thi frequ ncy a −SP wa present in the tl ird turn Our own m a urement were compared with those f Davi t al (1958)

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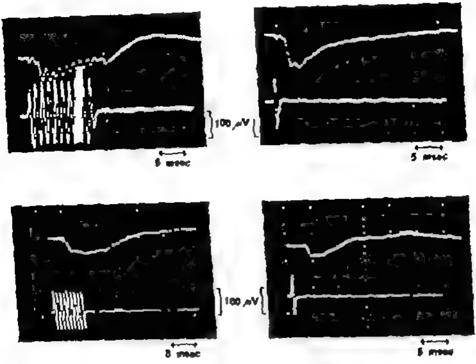

Fig. 6 Observation of the +SP and the −SP by increasing the number of ... measured in the apical turn of the cochlea. In the upper track the used stimulus frequency was 700 Hz, after 10 sinus the +SP is already formed. In the lower track the used stimulus frequency is 1600 Hz, no +SP can be formed now after increasing the number of si... SP formed

...tion of the condenser telephone receiver and for the lower sound pressures by the noise of the amplifiers. Still it was possible to cover a dynamic range of 40 dB in airborn sound, without distortion being introduced between 40 and 80 dB.

Since we had attributed such an important role to the "pure +SP" it was very interesting to measure the maximum values of this potential in the various windings by applying that frequency that would yield the maximum movement of the cochlear partition in that part of the cochlea. In Fig. 7 the best results are obtained in the third and second winding: the slope of the "pure +SP" is very steep when approaching the place where the cochlear partition must be in rest. The whole pattern must be related to von Békésy's envelope, although our curve is much sharper. In the apical and basal winding the measurement could not be as exact as before because of the small dimensions of the apical winding and the high resolving power for frequency of the basal winding, resulting in a close projection of the frequencies: the dimension of the electrode was here far too large to detect this fine analysing power.

Relations Between Frequency of the Stimulus Place of the Electrode and Polarity of the SP

It was easy to change the +SP into the −SP or vice versa by merely changing the frequency of the sound stimulus It appeared that there existed a specific frequency range, for a certain electrode position within which the SP shows the positive sign with a maximum value at a critical frequency If the electrode was situated in the third winding a maximum positive value was found at 2400 Hz by increasing the frequency of the sound stimulus to 2900 Hz, the SP changed its polarity completely into negative By lowering the frequency of the sound stimulus to 2800 Hz, the SP changed its polarity completely into negative By lowering the frequency from 2400 Hz down to about 1500 Hz, the SP stayed positive although its voltage reduced gradually There appeared to be a sharply defined edge on the high frequency side of the frequency band of positive polarity whereas the other side of that same band does not show such a clear zero crossing Outside the positive frequency band the SP was negative and remained so with a constant value throughout the whole frequency range above 2800 Hz (Fig 3) There was no doubt that the maximal +SP was reached in that part of the cochlea that corresponds with the point of maximal movement according to von Békésy s measurements in the cochlea *of the living guinea pig The −SP is found in that part of the cochlea* which is in rest during stimulation

These observations could be repeated for the other windings of the cochlea (Fig 7) The critical frequency that produced the change from −SP to +SP was in agreement with von Békésy s findings In the basal winding this critical frequency was about 11000 Hz, in the second third and fourth winding respectively 4500 2500 and 800 Hz. These measurements were clearly reproducible in one animal and even between different animals the critical frequency for a certain winding reproduced itself within a 15% tolerance A typical bandwidth could be found between the frequency maximum +SP value and the appearance of the −SP it always had a bandwidth of about 20% of the critical frequency under observation

Input Output Relation

In accordance with Davis work on the input–output relation measurements were performed on the −SP as well as on the +SP For the −SP a curve could be found analogous with Davis measurements (Fig 5) By plotting the maximum value of the +SP a similar curve could be found Keeping in mind that this +SP must be the algebraic sum of a hypothetical "pure +SP" and the ever present −SP the value of the +SP mentioned first had to be corrected for the −SP value (Fig 6) The input–output function was limited for high sound pressures by the mechanical dim n

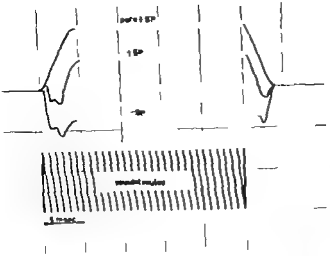

Fig. 9

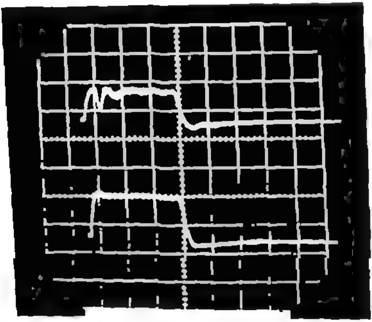

Fig. 9 b.

Fig. 9 (a) Schematical presentation of the +SP, the −SP and the "pure +SP". The "pure +SP" was found by subtracting the value of the −SP from the value of the +SP. (At present hypothetically found.) (b) The +SP and the "pure +SP" measured by differential electrode technique in the second turn of the cochlea. (Soundstimulus 4400 Hz.) In the lower track the "pure +SP" is clearly shown; the +SP in the upper track still contains the AP; the amplitude is smaller.

Duration of the Stimulus and the SP

If the signal merely consists of a few sinusoids (less than 5) only the action potentials can be observed revealing the first appearance of the −SP If the number of successive sinusoids surmounts 5 the formation of a +SP can be observed, preceding the −SP by the latency period The formation of the +SP apparently asks for a minimum number of sinusoids When listening to the monitor telephone receiver this was just the point where the click sound changed into a tonal sound

By observing the origin of the −SP by increasing the number of sinusoids, it was clear that the negative value of the signal beyond the N1 was caused by the added nerve action potentials The same could be done for the +SP after 5 sinusoids the signal turned positive and remained so independent of the number of sinusoids applied The large difference between the +SP and the −SP was very obvious with this method i e by increasing the number of sinusoids (Fig 8)

DISCUSSION

Our findings suggest that there must be different places of origin for the +SP and the −SP To give an explanation for both SP s a hypothesis is offered which separates both potentials as to location

When studying the structure of the −SP one is confronted with a striking similarity with that of the AP By applying a masking with white noise both the AP and the −SP can be reduced in amplitude the AP and the −SP start at the same moment and the input–output relation is similar for both potentials the −SP can be interpreted as a summation of the isolated asynchronous action potentials of the various nerve fibers Now we would like to suggest that the −SP is of neural origin, whereas the +SP must be located in another part of the organ of Corti

When considering the pure +SP which follows hypothetically from the observations of the +SP and the −SP one is struck by the fact that it runs synchronously with the CM there is no latency The pure +SP" has been constructed by subtracting the −SP from the +SP later on the same procedure was electrically performed by using differential electrodes in the scala tympani and vestibuli following a very well known technique In this way the −SP was eliminated from the measured +SP leaving back the "pure +SP On the upper track on the oscilloscope screen the registration of the +SP was seen the lower track showed the pure +SP" There was a striking resemblance between the constructed pure SP" and the electrical measured pure +SP (Fig 9 *a* and 9 *b*) The maximum of the "pure +SP" is found in that part of the cochlear partition that is in maximum movement during stimulation The "pure SP" seems to be

Membran während des Tonreizes sich nicht bewegt Es wird behauptet dass das +SP und da −SP in verschiedenen T ilen des Cortischen Organs erregt wird Da die Latenzzeit des −SI gen u dieselbe ist wie die des AP's, wird angenommen, dass das −SP in Summation der s nchronen Aktionspotentiale ist. Das +SP fing gleichzeitig mit dem CM n und hatt k ine Laten eit. Das sa bere SP" das auf theoretischen Gründen berechnet ist, durch die W rte des −SP's on den Wert n des +SP's in Abzug zu bringen wird in Übereinstimmung mit der Theorie Davis l in Spa nngsleck durch das Organ von Corti während der ton len Anregung betrachtet.

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more closely related with the movements of the basilar membrane than is found for the −SP

Davis stated in 1960 that in considering the stimulating mechanism of the haircells one should assume a current from the scala media (+80 mV) through the haircells to the scala tympani (0 mV) Thus the organ of Corti should be considered as a variable resistance the value of which is directly related to the movements of the basilar membrane Later investigations by Christiansen (1964) stated that there are protein structures in the lamina reticularis, which can act as a variable resister by form alterations

Based on the above assumption the pure +SP and the +SP which *is measured right under the basilar membrane in the scala tympani* should be regarded as the potential difference caused by the leakage current from *scala media to scala tympani as a consequence of the movements of the* basilar membrane and proportional to them Since summating is now out of the question for the +SP the introduction of a new name is required such as the Dynamic DC Potential The term Summating Potential can be maintained for the −SP

If we return now to the relationship between the localization of the +SP and the frequency of the sound stimulus, more can be said about the area involved In our experiments it was found that the bandwidth in which the +SP changed into the −SP was about 15% of the frequency at which the maximum +SP value occurred This value of 15% resembles the value of the critical bandwidth in man as measured by Fletcher (1940) Zwicker (1957) Greenwood (1961) and Plomp (1964) There is a strong resemblance between the human and guinea pig cochlea so it can be concluded that the bandwidth of polarity change of the SP could be identical with the critical bandwidth as measured in man

ZUSAMMENFASSUNG

Viele widersprechende Auffassungen über das Entstehen des Summating Potential" sind *in den bisherigen Veröffentlichungen — nach der Entdeckung* durch Davis und Mitarbeiter (1950) — erschienen Die Ergebnisse Davis und Mitarbeiter schienen einen Zusammenhang zwischen der Reizfrequenz der Polarität des SP s und der Stelle der ableitenden Elektrode aufzuweisen Bisher hat man diese Voraussage jedoch nicht beweisen können Es wurden nicht polarisierbare Elektroden verwendet um die Änderungen des SP s *in den verschiedenen* Windungen der Schnecke des Meerschweinchens zu finden beim Applizieren eines tonalen Reizes Die Parameter Frequenz Intensität und Dauer konnten dabei geändert werden In allen Windungen der Cochlea konnte eine nachweisbare Änderung in der Polarität des SP gefunden werden sobald die Reizfrequenz um eine gewisse Zahl geändert wurde *Die Maxima des* +SP werden *dort ge*funden wo die basiläre Membran die maximale Bewegung durchführte nach von Békésy Das *−SP wird in* der Cochlea an der Stelle gefunden wo die basiläre

INFLUENCE EXERTED ON AUDITORY FATIGUE BY SOME CALMATIVES AND STIMULANTS OF THE CENTRAL NERVOUS SYSTEM

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A remarkable decrease f th i ten ity nd duration of auditory f tigue has been found on dministrati f atarax and m probamat d it ppears that th effect produced by these drugs through the reticular formation Admini tration of luminal brought about but a small decrease particula ly in young people Caffein shortened and alleviated the f tigue its ction being strikingly dependent on th ge of xaminees. No effect ha been detected i the case f lobelin and neither intensity no duration of the fatigue were decreased on dministration of placebo The results bt ined seem t point t ignificance f the reticular formation in th mechanism f ditory fatigue

A irritation of the audit ry rgan with a prolonged or over intense sonic stimulu leads to ne of the three effects adaptation fatigue or trauma. A ha been pointed out by a serie of authors, auditory fatigue and audit ry daptation constitute two different phenomena of a transitory decrease in sensitivity of the organ (von Békésy 1960 Hahn, 1962 Langenbeck, 1960 Lüscher 1952 Sielużycki, 1962 Szpunar 1963 and others) An appellation f by timulus and post stimulus adaptation has been proposed by othe auth rs to tell the two phenomena apart (Capell & Montserrat 1961 M spétiol, 1962 Portmann & Portmann, 1954 and oth rs.) The adaptation i a physi logical phen menon, a beginning of a new functional period in altered conditi ns. It remains unchanged as long as a st mulus is pplied and v nishes quickly when the irritation is stopped (Gouvry 1961 Led ux & Paepe 1961) The auditory f tigue is a pathological phenomen n and ignifies a temporary injury to the organ resulting f m an er-int nse irritation. The injury h wever becomes manifest after certain i pse f time foll wing the withdrawal f the irritation. In particula condition the fatigue persist and is spoken of as a trauma (hylin, 1960)

In pit of exten ive research opinion still vary as to where and how uditory f tigu is gen rated. Acc rding to Békésy it devel ps at the point f pplication f the stimulus in the peripheral receptive organ, which

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A remarkable decrease of the intensity and duration of auditory fatigue has been found on administration of atara and meprobamate and it appears that the effect is produced by these drugs through the reticular formation. Administration of luminal brought about but a small decrease particularly in young people. Caffeine shortened and alleviated the fatigue, its action being strikingly dependent on the age of examinees. No effect has been detected in the case of lobeline and neither intensity nor duration of the fatigue were decreased on administration of placebo. The results obtained seem to point at a significance of the reticular formation in the mechanism of auditory fatigue.

An irritation of the auditory organ with a prolonged or over-intense tonic stimulus leads to one of the three effects: adaptation, fatigue or trauma. As has been pointed out by a series of authors, auditory fatigue and auditory adaptation constitute two different phenomena of a transitory decrease in sensitivity of the organ (von Békésy 1960, Hahn, 1962, Langenbeck, 1960, Luscher 1952, Sielużycki, 1962, Szpunar 1953 and others). An appellation of "by-stimulus" and post-stimulus adaptation has been proposed by other authors to tell the two phenomena apart (Capella & Montserrat, 1961, Maspétiol, 1962, Portmann & Portmann, 1954 and others.) The adaptation is a physiological phenomenon, a beginning of a new functional period in altered conditions. It remains unchanged as long as a stimulus is applied and vanishes quickly when the irritation is stopped (Gomiry 1961, Ledoux & Paepe 1961). The auditory fatigue is a pathological phenomenon and signifies a temporary injury to the organ resulting from an over-intense irritation. The injury, however, becomes manifest after a certain lapse of time following the withdrawal of the irritation. In particular conditions the fatigue persists and is spoken of as a trauma (Kylin, 1960).

In spite of extensive research opinions still vary as to where and how auditory fatigue is generated. According to Békésy it develops at the point of application of the stimulus in the peripheral receptive organ, which

is the basilar membrane. Alternating intensity of sound produces via osmotic processes, a change in the concentration of the chemical components and this in turn results in an electric impulse stimulating the nerve fibres. According to Gouvry, Langenbeck, Lüscher and others adaptation also takes place in the cochlea and probably depends on a mechanical change in the elasticity of the tectorial membrane or Corti's organ, while fatigue depends on the bio-electrical processes at this level. Electro-acoustic examination of the cochlear potentials (Ruben & Sekula 1961) has shown that the auditory fatigue varies in the presence of other stimuli, visual, olfactory, etc. and also when the reticular formation is irritated. According to Brunetti, Maspétiol and Paiva the fatigue is governed by the central nervous system, particularly the reticular formation. There are many methods of testing the auditory fatigue and auditory adaptation as the tests of Peyser, Wilson, Theilgard, Hood, Carhart, Feldman and others show. The purpose of these tests was to establish personal vulnerability to an accoustic injury. A majority of the experiments however have consistently confirmed that there is no interrelation between the degree of auditory fatigue and the personal vulnerability to an acoustic injury.

The effect of pharmacological agents on hearing and the behaviour of auditory fatigue is not yet well known. Results obtained by many authors point at a strong influence of the vegetative system on auditory fatigue (Lüscher 1952, Plester, Seymour and others). The works of Jankowski *et al.* (1956, 1955, 1962) show that the sympathetic system has but a small direct share in the preservation of the microphonic potentials and that its indirect influence, which consists of disturbance of the blood circulation in the cochlea and, consequently, the oxygenation process, is much more important. Morphine, according to Radzimiński, does not influence the tonal threshold of hearing and the better understanding of speech produced by it should be ascribed to its effect on the central nervous system. In recent years particular attention has been given to the drugs which decrease the reaction of the organism to harmful stimuli and reduce the metabolism in the nerve cell. These drugs constitute a very numerous group and are called by the common name of ortholomic agents or tranquillizers. Examination of the way in which they operate has disclosed that the origin of their action falls within the reticular formation (formatio reticularis) responsible for the state of vigilance.

Recent researches (Hahn, Magoun, Sadowski and others) seem to suggest that the reticular formation plays an important part in promoting and moderating the functions of the nervous system. Hernandez-Peon, Scherrer and Jouvet have found (after Sadowska) that irritation of the reticular formation in a cat produces a restraining effect on the functions of the cochlear nucleus. Irritation of Rasmussen's olive-cochlear fasciculus in the brain stem has been found by Calambos to restrain auditory signals in the cochlea. Ruben & Sekula discovered that the auditory response becomes cancelled at the level of auditory organs, corpora geniculata or

auditory nerve depending on the intensity of an electric stimulus operating on the olive-cochlear fasciculus According to Hernandez the fasciculus constitutes the terminal element of an afferent system contained between the cortex and the cochlea As it becomes irritated, the microphonic potentials increa e as a result of the disengagement of acetylcholine in the cochlea (Gisselsson & Sörensen, 1950) According to Glotty the reticular formation becomes less sensitive on administering a tranquillizer In Polish medical literature the problem of the application of tranquillizing drugs for labyrinthine and extralabyrinthine diseases was discussed by Kossowski et al (1962) By administration of these drugs they obtained a decrease of tinnitus and the tests of adaptation showed an increase of the b-field in the adaptogramme of the Feldman test which reflects the efficiency of the cochlear nerve Also the researches of Hahn & Scarzella confirm that largactil decreases remarkably the time of threshold decay which indicates the significance of the reticular formation in the mechanism of auditory fatigue

RESEARCH

Examinations were carried out on the staff of the 1st Laryngological Clinic, PG.M.S. in Warsaw Twenty persons were examined, their ages ranging from 18 to 60 years. The examinees were subdivided into four age groups

1st group—below 21 years
2nd group—21 thr ugh 40 years
3rd group—41 through 50 years
4th group—51 through 60 years.

All th w uld be examinees were asked questions about illnesses of the auditory organ nd upper respiratory tract which they had suffered and about the drugs and stimul nt which they had been taking. Those selected for the test were healthy people. Of stimulants, they were habitually drinking coffee in large and medium quantities (1 to 6 cups a day) and a majority m ked igarettes (about 20 a day)

The test were carried out with the following gents (a) calming agents atarax, meprobamate luminal (b) stimulating agent caffeine strychnine, lobeline

Fo the purpose of control each of the examinees wa given placebo mylum) d wa subjected t tests analogous to those performed after th dmin stration of the drug specified above Among the calmatives particul attention was paid to tranquillizers, selecting those which produce least side ffect and whose influence on hearing had not been tested before The choice f luminal wa i spired by it somniferous action. It seemed interesting to see if this cti n would have any influence on udit ry f tigue Among the drug f the second group strychnine with

its strong stimulating action, seemed likely to have some influence on the fatigue It was singled out because it makes the reflex arcs more sensitive and increases the sharpness of the sense Lobeline was chosen because it affects the central nervous system indirectly via reflex with sinus caroticus, and its stimulating action is thus different from that of the two drugs mentioned previously

METHOD

The tests were carried out in a room of mediocre silence and using a Polish made audiometer Audiomatic Elza A modified version of the Peyser test was applied the modification consisting in transmitting for 8 minutes to the ear a tone of 1500 Hz and an intensity of 75 dB above a predetermined threshold and subsequently determining the thresholds for both the irritation and neighbouring frequencies, i e 1000 2000 and 4000 Hz. The first check was done immediately on switching off the irritation tone and the next ones at every two minutes until the initial threshold values reappeared The hearing threshold of the test frequency was accurately determined before each test

The above modification was introduced because it rendered the tests simpler and in comparison with other methods, the elevation of the threshold was relatively great and long lasting An average magnitude of auditory fatigue obtained with this method amounted to 20 dB with a duration of 8 minutes In the Peyser Theilgard and Wilson tests a 5 dB increase of the threshold is treated as standard while a 10 dB difference can already be suspected of being pathological yet such small values were unacceptable with the Audiomatic Elza A scale division there is 5 dB and a difference of 5–10 dB may well be considered as the limit of error

Starting from the assumption that auditory adaptation and auditory fatigue constitute two different phenomena the author's task being to estimate the influence of some agents affecting the central nervous system on the fatigue only all the tests aiming at the determination of the adaptation have been excluded from this work

Each of the examinees was primarily subjected to two empty tests, meaning tests without any of the drugs specified above The purpose of such a procedure was to mark out a standard auditory fatigue The results obtained although varying in different persons proved to be in any given examinee, constant ; provided that the tests were conducted under the same conditions and at the same time of day The intensity and duration of the fatigue were subject to large changes in the presence of additional psychical and physical stimuli The best illustration of this is given by the diagram of auditory fatigue in a nurse after 3 days of night duty in comparison with the normal curve plotted for this person The auditory fatigue here amounts to 25 dB/12 min and 15 dB/6 min respectively

On establishing the standard for a given person the next step was to test the auditory fatigue after administration of one of the agents specified below The examinees were not told which drug they were taking

Calming drugs

Atarax ((1 p-chloro-benzyhydrolo-4) 2 2 hydroxy (-ethyl) piperazine hydrochloride)) The tests were performed 30 min after oral administration of a 10 mg dose of the agent

Meprobamate (2 methyl-2n propyl-1,3-propandiol bicarbominate) Auditory f tigue was tested 30 min after oral administration of a 0 4 g dose

Luminal (5-ethyl-5 phenyloborbituric acid) The auditory fatigue tests were performed 90 min after oral administration of a 0 1 g dose

Stimulating drugs

Strychnine (an alkaloid occurring in different species of plants of the genus strychnos) The auditory fatigue tests were performed 20 min after hypodermic administrati n of a 0.002 g dose

Caffeine (1,3,7-trimethyl xanthine) The tests were performed 15 min after oral administration of a dose of 0.2 g. It was a strictly observed rule that the examinee should not drink coffee on the day the test was per f rmed

Lobeline (an alkaloid derivati e of piperadine) Auditory fatigue was tested immediately fter hypodermic administration of a dose of 0 003

In order t control reactions the tests were performed after administra tion of placebo. Between two consecutive tests there were intervals of at least 4–7 days. Each of the examinees was additionally subjected to one control test f tigue with no drug administered In this way each person underwent 10 tests of auditory fatigue and the total number of tests was 200

RESULTS

The tests ha e shown that the greatest increase of the threshold takes place with the frequency of th irritating tone The increase observed with 4000 Hz was equal to, and sometimes e n less than, that of the irritation frequency Th biggest values bove the thresholds were detected im mediately fter disconnecting the irrit ting signal nd after 2 min the fatigu fell down to 10–5 dB abo e the threshold. The increase of the threshold with the f equency of 1000 Hz, i.e maller than the irritation n h d minimum, sometimes undetectable values.

An nalysi which was m de after applicati n of the calming agents ha hown that none f them had any influence on the threshold of hearing On the other hand, a very strong effect on auditory fatigue has been f und with atarax and mep obamate Both these drugs tend to con plen usly diminish intensity nd durati n of the f tigue and seem to act

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Each of the examinees was primarily subjected to two "empty" tests, meaning tests without any of the drugs specified above. The purpose of such a procedure was to mark out a standard auditory fatigue. The results obtained, although varying in different persons, proved to be in any given examinee constant, provided that the tests were conducted under the same conditions and at the same time of day. The intensity and duration of the fatigue were subject to large changes in the presence of additional psychical and physical stimuli. The best illustration of this is given by the diagram of auditory fatigue in a nurse after 3 days of night duty in comparison with the normal curve plotted for this person. The audtory fatigue here amounts to 25 dB 12 min and 15 dB/6 min respectively.

F g. 3.

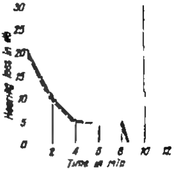

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FIG. 3. The common mean of ditory f tigue fter the stimulati g gents. ——— Normal (hearing loss 20 dB, time 8.2 min) l minal (hearing loss 16.5 dB, time 7.4 min) ---- meprobamate (hearing loss 11 dB, time 4.5 min); tarax (heari g los 11dB, time 3.6 min)

FIG. 4. A diagram I uditory f tigue fter placebo. ——— Normal Placebo.

cortex. The hypothesis of central action gains further support by the fact that the tests have revealed no effect on the threshold of hearing This falls in with Laborit s discovery in his experiments after Jus, that tranquillizers can moderate functions of the central nervous system by slowing down reactions to harmful stimuli. The decrease of auditory fatigue observed with atarax and meprobamate can be exactly an effect of this slowed-down reacti n of the reticular formation to a harmful, over intense sonic stimulus, while the sharpness of hearing itself being a reaction to a threshold and thus harmless, stimulus, remains unaffected by these drugs Also Glotfelty maintains that tranquillizers can decrease the sensi tivity of the reticular form tion to sensory stimuli The results seem to prove th t the reticular formation plays an important part in the mechanism of auditory fatigue and these results are compatible with those obtained by Hahn after the administration of largactil. Yet it should be emphasized that a maj rity f the examination of auditory fatigue confirm it to be localized in Corti s organ Therefore it seems that, while the results testify to an influ nc of the reticular f rmation on the mechanism of fatigue certain effect f tranquillizers on the peripheral perceptive organ of hearing cann t be excluded. Such an effect wa suggested by the results obtained by Kossowski *et al* in treating Menière disease with orthotomic agents They obtained better efficiency of the cochlear nerve which was ind c ted by an increase of the b-field of the adaptogramme in the Feldman test.

Th res lt discu sed h re show a remarkabl decrease in the intensity and durat on f auditory fatigu on administering atarax and meprobamate which, con id ring thei rigin of action, can be a proof of an essential influence of th reticular formation on the mechanism of auditory fatigue

In ord to acc rately determine the localization of the auditory fatigue

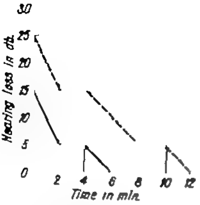

Fig 1

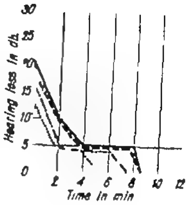

Fig. 2

Fig 1 A diagram of auditory fatigue after 3 days of duty ——— Normal - - - - after 3 days of duty

Fig 2 The common m an f auditory fatigue aft r the calming agents. ——— Normal (hearing loss 20 dB, time 8.2 min); - - - - lobeline (hearing loss 18.25 dB, tim 8.2 min); - - - strychnine (hearing loss 16 75 dB, time 7.6 min) caffeine (hearing loss 13 dB, time 5.2 min)

in a fairly similar way They can in some people produce a slight feeling of sleepiness According to the results obtained luminal has a rather limited influence on fatigue. In young people however a certain very small effect can be traced

An analysis of the results obtained with the stimulating agents proves them to be of no effect on the threshold of hearing On administration of caffeine auditory fatigue becomes less intense and durable but the effect is distinctly dependent on the age of the person who has taken the drug However it should be remembered that all the examinees were habitually drinking coffee Strychnine has been found to affect auditory fatigue to a certain minimum degree, without influencing the sharpness of hearing The results obtained with lobeline prove this drug to be totally devoid of influence on auditory fatigue

For the purpose of control all the examinees were subjected to a test of auditory fatigue after administration of placebo (amylum) No decrease of intensity nor shortening of duration of the fatigue were detected although the examinees did not know which drug they were taking It is worth mentioning that many examinees were complaining of sleepiness after placebo however with no effect on the results

DISCUSSION

Among the results obtained the big influence exerted on auditory fatigue by atarax and meprobamate deserv s particular attention The mechanism and origin of the action of these agents are not yet sufficiently known The results seem to reflect their influence on the reticular formation where harmful stimuli are liable to become dispersed and emitted onto the

2. The influence exerted on audit ry fatigue by luminal is of a minimum degree and it can mainly be detected in young people

3. After administration of caffeine auditory fatigue decreases, particularly in young people

4 The influence observed with strychnine was minimum

5 No influence on auditory fatigue has been discovered after the ad ministration of lobeline

6. None of the agents tested has been found to affect the threshold of hearing.

7 In none of the examinees has any decrease of the intensity and dura tion of auditory fatigue been shown after placebo was administered.

8 The results obtained seem to indicate an influence of the reticular formation on the mechanism of auditory fatigue

ZUSAMMENFASSUNG

Es wurde eine hervorragende Verml lerung und Verkürzung der Dauer der Hörermüdung bei Anwendung von Atara und Meprobamat festgestellt. Da scheint von der Wirkung dieser Heilmittel durch die F rmati retleulari abhängig zu sein Nach der Anwendung von Luminal k mmt nur ein geringe Verminderung der Hörermüdung vor besonders bei jungen Menschen I ter der Wirkung von Coff in kommt in Verkürzung und Verminderung der Hörermüdung vor wobel in bed utender Zusammenhang mit dem Alter der untersuchten Perso en festgestellt wurde Die Anwendung on Lobeli weist keinen Einfluss auf die Hörermüdung auf E wurd weder ei Verminderung noch eine Verkürzung der D uer der Hörermüdung festgestellt

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and evaluate the effect of tranquillizers it would be interesting to test their influence on the fatigue in different illnesses of the receptive auditory system. It would also be interesting to test the effects of other tranquillizers, tranquillizers of different chemical structures and different origins of action.

The effect of tranquillizers seems to depend more on their calming action than on the somniferous one which in turn is evidenced by the relatively small influence exerted on auditory fatigue by a somniferous dose of luminal. The fact that luminal affects mainly the cortex and not the reticular formation, may also be of some account here as the latter appears to have the biggest importance in the mechanism of fatigue. The alleviation of fatigue can probably be explained by its calming effect on the central nervous system and ensuing restraint of the senso-motory function of cortex.

Among the stimulating agents caffeine has been found most effective particularly in young people. The result seems to depend on a stimulating effect of caffeine on the sensory function of the brain as well as on a certain precipitation of psychical reactions. As caffeine acts in a different way than the tranquillizers, its effect on the fatigue may be viewed as paradoxical, but it is probably conditioned on the vasomotory processes in the central nervous system. The milder reaction of older people should in the first place be associated with the fact that they have grown accustomed to caffeine and also with the general abatement of reactivity to administered agents observed with the progress of age.

The results obtained on the administration of strychnine prove that its effect on fatigue is a minimum one. Nor has there been any change detected in the threshold of hearing although according to Choróbski, Dadlez, Hano and Supniewski strychnine sharpens the functions of the sense organs. However, it should be emphasized that the examination involved only separate injections of small doses of strychnine, the tests being performed on volunteers (doctors, nurses, ward attendants) who could not be persuaded into taking the agents for a longer time. On the administration of lobeline neither threshold of hearing nor auditory fatigue have been found affected. The effect of this agent through sinus caroticus is minimum and short lasting. The absence of changes in the auditory fatigue after administration of placebo seems to deny the supposition that a psychical disposition alone could have been of any effect on the results obtained with the pharmacological agents.

CONCLUSIONS

1. A remarkable decrease in the intensity and duration of auditory fatigue has been found after atarax and meprobamate were administred independently of the age of examinees.

TRANS-ORAL MAXILLECTOMY

Radical Resection without Facial Incision

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Trans-oral maxillectomy requires no facial incision and reduces deformity thereby decreasing the psychological trauma f radical surgery The duration of surgery i shortened drastically *En bloc* maxillectomy and orbital exenteration i possible Wound healing is better The survival time f 222 pati nts with ma illectomy was in estigated nd the prognosis wa found t be better i patients treated by the tra s-oral approach The operative technique can easily be learned by a yone killed in otorhinolaryngological surgery

INTRODUCTION

From the viewpoint of advancement in the treatment of maxillary malignancies the study of Öhngren (1933) should be revaluated The pathological study by Ringertz (1938) and the study on the prognosis in radical operated maxillary cancer cases by New & Cabot (193.) are also worthy of n te More recently a large clinical study by Larsson & Mårtensson ppeared (19.4) in which they reported 3 cases which were operated by electrosurgical means.

The treatment of maxillary cancer has been widely discussed and reported In general, surgical methods are cla ified into two primary categ ries comparatively conservative one utilizing electrocoagulation as described by H lmgren in 1925 and a more radical excision through an external facial incision as has long been advocated by many surgeons. Method and results of m xillectomy or upper jaw resection, through ex ternal faci l in isions hav been reported by Tabb (1937 1959) Hendrick (19.8) Barbosa (1961) and Pietrant ni (1960)

I dditi n to urgery there i a general tendency to treat maxillary c n with irradiati n either before o after maxillectomy

E en xtensive tis ue removal does n t as ure a favourable prognosis in m ny cases f maxillary cancer Many outpatients in clinical practice ha exten ion of their disease far beyond ur expectations

Th hi t ry of maxillectomy may be traced back to Akoluthus in 1630 and many different facial inci ion have been advocated since Joseph Gensoul in 1820

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TABLE 3 *Initial symptoms*

Symptoms	Number of cases	
Nasal obstruction	78	31.2
Nasal bleeding	35	14.0
Toothache	32	12.8
Cheek pain	29	11.6
Cheek swelling	29	11.6
Nasal discharge	26	10.4
Temporal pain	7	2.8
Palatal swelling	5	2.0
Cheek paresthesia	3	1.2
Epiphora	2	0.8
Diplopia	1	0.4
Dull sensation in head	1	0.4
Intranasal tumor formation	1	0.4
Palatal fistula	1	0.4

TABLE 4 *Objective symptoms*

Symptoms	Number of cases	
Intranasal tumor	170	68.0
Cheek swelling	147	58.8
Choanal tumor	84	33.6
Palatal swelling or ulcer	40	16.0
Exophthalmos	30	12.0
Canine fossa tumor	24	[illegible]
Alveolar tumor	4	1.6
Visual disturbance	3	1.2
Oculo-motor disturbance	2	0.8
Trismus	2	0.8

author's trans-oral maxillectomy were performed in the Kurume University Hospital, and those about 40 cases were not included in the present series.

The present series of radical maxillectomies now consists of 250 cases which have been operated on during the 15-year period between 1946 and 1961. This series consists of 120 patients who had trans-oral maxillectomy and 120 patients who had the usual external facial incision. The remaining 10 cases had a radical Denker's procedure and are not included in this discussion. Therefore we feel that an impartial comparison of the two modes of treatment can be made (Table 1).

The age and sex distributions are as follows (Table 2). There were 159 males and 91 females. The peak age incidence was in the fifth decade, with the fourth and then the sixth decades being the second and third highest respectively.

The Symptoms of the Maxillary Cancer

There are no reliable early symptoms. In our series, nasal obstruction occurred in 78 cases (31.8%), epistaxis in 35 cases (14.0%), toothache in 32 cases (12.8%) and cheek pain and swelling were noted in 29 cases (11.6%) (Table 3). The most frequent objective signs were the presence of tumor in the nasal cavity in 170 cases (68.0%) and swelling of the cheek in 147 cases (58.8%) (Table 4).

Diagnosis by Means of Circus Tomography

Circus tomography as described by Matsukawa in 19 has been used to define the precise extension of the tumor. We take maxillary tomograms with seven films at 1.0 cm intervals in the frontal plane and five films at 1.0 cm intervals in the sagittal plane. The cut is very thin and free from

TABLE 1 *Number of operated cases of maxillary cancer during 1946–1961 in the Department of ORL Kyushu University*

Year	Trans-oral	Facial incision	Denker's operation	Total
1946	0	4	0	4
1947	0	9	0	9
1948	0	5	1	6
1949	0	12	1	13
1950	1	[illegible]	2	19
1951	0	[illegible]	0	10
1952	8	8	1	17
1953	7	9	1	17
1954	3	10	0	13
1955	7	12	0	19
1956	0	11	0	11
1957	14	11	0	25
1958	22	0	3	25
1959	11	[illegible]	1	12
1960	13	6	0	19
1961	28	0	0	28
Total	120	120	10	250

However most radical maxillectomies have utilized an external facial incision except the electrocoagulation method of Holmgren and the radical procedure of Denker. The author's trans-oral maxillectomy was reported in 1949 and 1950 since that time trans-oral exenteration of the orbital content has also been performed in indicated cases. The earlier cases of

TABLE 2 *Age and sex-distribution in cases of maxillary cancer*

Age	Number of cases	Male	Female
17	1	1	0
21–25	3	1	2
26–30	11	6	5
31–35	11	10	1
36–40	21	14	7
41–45	44	25	19
46–50	23	[illegible]	
51–55	[illegible]	30	1
56–60	35	1	14
61–65	[illegible]6	1	11
66–70	18	11	7
71–75	11	8	3
77	1	1	0
Total	250	159	91
		63.6	36.4

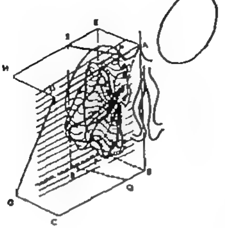


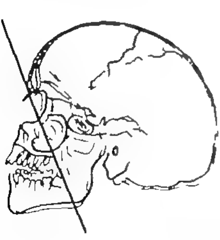
FIG. 2. Reconstructed t mor figures from tomograms.

plane one can divide the front middle region of the skull into easily discerned segments the anteri r inferior block (A) the posterior superior block (P) through Öhngren s malignancy plane the medial block (m) and the lateral block (l) through the "Piriform-pterygoid plane" (Fig 5 a)

These four block of the front middle region of the skull may be used in the classification of stages of invasion (Fig 5 b) The con ponent struc tures of these maxillary blocks are as follows

Am (Anterior inferior medial) nasal cavity palate

Al (Anterior Inferior-lateral) maxillary sinus, alveolar process and zygomatic bone



F 3.

F a. 4

FIG. 3. Malignancy plane (Öhngren)

FIG. 4 Piriform-pteryg id plane.

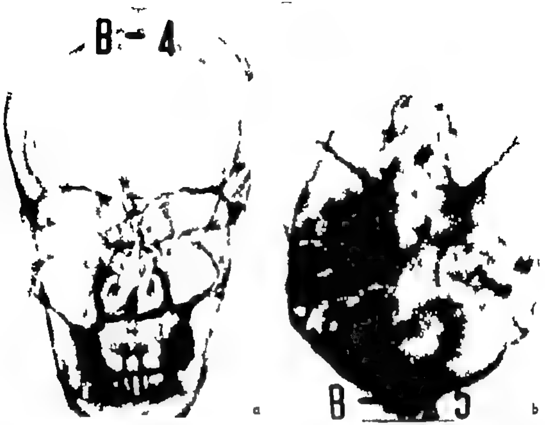


Fig. 1 a Frontal section at 4 cm apart from anterior facial surface by a case of maxillary cancer of the right side
Fig. 1 b Axial section at 12.5 cm apart from head surface by the same case of maxillary cancer

distortion The tomo films can better be visualized by the use of logetronography (Fig 1 a b) These tomograms form the basis for our classification of the area of invasion which will be discussed later together with reconstructed figures of the cube effect (Fig 2)

Classification of Tumor Extension by Use of Invasion area type

It would be desirable to have simple criteria for the classification of the invasion characteristics of maxillary cancers Many classifications are too detailed and complicated to be practical Öhngren's classification was founded on a simple anatomical basis however it lacks bilateral standardization (Fig 3) Ishrat Husain (1960) divided the head with vertical section through the pupil of the eye but the localization of the pterygopalatine fossa and the pterygoid process is not clear I should like to suggest that the principal shape of the maxilla is an inverted pyramid Since the medial wall of this bony construction is in a vertical plane I have imagined a plane and called it the "Piriform pterygoid plane" It is parallel to the body axis and passes through the margin of the piriform aperture and the lateral lamina of the pterygoid process (Fig 4) This is a more satisfactory way to consider the anatomic area and by using this vertical

TABLE 5 *Classification of cases according to the invasion area type*

Invasion area type	Number of cases		Group	Cases in group	of group
Am	12	4.8	A	77	30.8
Al	40	16.0	(Anterior)		
Aml	25	10.0			
Pm	35	14.0	[illegible]	41	16.4
Pml	6	2.4	(Posterior)		
AmPm	12	4.8			
AlPm	84	33.6	AP	132	52.8
AlPml	10	4.0	(Anterior		
AmlPm	[illegible]	8.8	Posterior)		
AmlPml	4	1.6			

when I adopted a new approach to maxillary cancer. My first experiences of trans-oral *en block* maxillectomy were devised by wound treatment after the maxillectomy by means of usual facial incision method. With further experience the *en bloc* exenteration of orbital contents followed as a natural course in development of the technique.

Method of Trans-Oral Maxillectomy

(a) *Palatal and alveolar incisions of the mucous membrane*

The upper anterior incisor of the affected side is removed. A semicircular D-shaped incision is then made through the defect left by extraction of the upper incisor tooth and is extended to the outside of the alveolar arch and to the middle of the palate—thereby demarkating an area which includes two-thirds of the palate on the affected side.

(b) *Separation of the maxilla*

The anterior bony surface of the maxilla is widely separated from overlying soft tissue. If tumor extends through the bone anteriorly electrosurgical separation of the tissues should be performed to preclude the possibility of spreading tumor cells.

(c) *Separation of contiguous bony structures*

Initially zygomatic process of the maxillary bone is freed outside its suture line with a side electrical saw and taking care not to injure the lateral contents of the orbit. Then the frontal process of the maxilla is obliquely cut toward the median sagittal plane and separation of the palate thus performed (Fig. 6).

(d) *Dissection of remaining structure*

Subperiosteal dissection of orbital contents is now carefully performed with a curved elevator. Posterior separation of the maxilla is facilitated

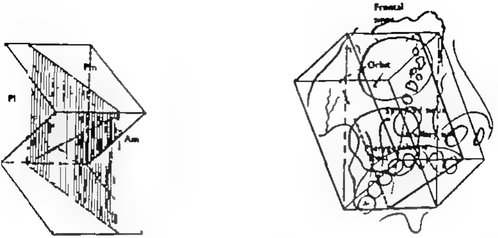


Fig 5a

Fig 5b

Fig 5 Invasion area type (a) Fundamental division of the invasion area type. Malignancy plane (Öhngren). Piriform-pterygoid plane (b) Paranasal sinuses projected into invasion area types.

Pm (Posterior Superior medial) frontal sinus, ethmoid sinus, sphenoid sinus, pterygopalatine fossa

Pl (Posterior-Superior lateral) maxillary tuber infratemporal fossa, orbita

Classification of the 2?0 cases of maxillary cancer according to this system yielded the following results (Table 5)

The majority of these cases were found at radical operation to be in the extensively infiltrated combined anterior posterior group

The Operative Procedure of Trans Oral Maxillectomy

It has been generally accepted that the results of surgical treatment of malignancies of the upper jaw are poorer than that of laryngeal cancer One of the obvious reasons for the relatively good prognosis in cases of laryngeal cancer is that the larynx is contained within a cartilagenous hard shell which restricts extension of the tumor It should thus follow that the bony barrier to the extension of maxillary cancer would be even more efficient However this is not so and the majority of our cases were found to be far advanced when they came to our clinic This fact may be one of the key points in the problem to be settled

Many people feel that prophylactic exenteration of the orbital contents improves the prognosis however scrutiny of our results demonstrates many long term survivals among patients in whom orbital exenteration was not done

Today almost all surgeons use the traditional facial incisions for maxillectomy Most of these methods closely resemble each other and are based on the common principle of excision of anterior facial soft tissue My initial experience was also with such methods until after World War II

Fig. 7. Resected maxilla of the left side. (a) Viewed from medial. (b) Seen from above. (c) Viewed from lateral.

FIG 6 Separati n of pal t

by the use of a trowel like elevator or similar shaped chisel Thus, even the firm bony union with the pterygoid process can easily be separated

The preceding maneuvers will allow considerable mobility of the maxilla The lateral wall of the affected nasal cavity should be cut at the level of the middle turbinate attachment

(e) *Removal of maxilla*

By applying pressure the maxillary body is pushed inferiorly and laterally It is grasped with large forceps dissected free of surrounding muscles, and removed *en bloc* Through débridement of remaining shredded soft tissue is now accomplished with large mucous membrane cutting forceps If invasion of the pterygoid muscles is noted they must be completely resected Cleaning of the pterygopalatine groove is particularly important The superior portion of th lateral nasal cavity including ethmoid and sphenoid cells should be opened

The above-mentioned structures, excepting radical neck dissection can also be removed *trans-orally but I prefer to sav th eye ball if possible* (Fig 7)

After local cleansing with Tespamin solution (anti-cancer drug) and penicillin solution the cavity is tightly packed with a rubber bag containing alginate hydrocolloidal paste in rder to prevent facial retraction and wound shrinkage

TABLE 6. *Recurrent cases of maxillary cancer classified according to the type of operative procedure*

Invasion area type	*Operative procedures of maxillectomy* Trans-oral			Facial incision			Denker					
	Total	Recurrence		Total	Recurrence		Total	Recurrence		Total	Recurrence	
Am	6	2	33.3	0	0		5	1	20.0	11	3	27.2
Al	19	8	42.1	15	4	26.6	1	0		35	12	34.3
Aml	9	4	44.4	15	8	53.3	1	0		25	12	48.0
Pm	26	13	50.0	10	7	70.0	2	2	100.0	34	22	64.7
Pml	3	3	100.0	2	0		0	0		5	3	60.0
AmPm	3	2	66.6	7	4	57.1	1	0		11	6	54.5
AlPm	17	10	58.8	57	31	54.3	0	0		74	41	55.4
AlPml	5	1	20.0	3	1	33.3	0	0		8	2	25.0
AmlPm	8	5	62.5	10	8	80.0	0	0		18	13	72.2
AmlPml	0	0		1	1	100.0	0	0		1	1	100.0
Total	92	48	52.1	120	64	53.3	10	3	30.0	222	115	51.8

13.0% within 4–6 months, only 14.0% from 6–12 months. Therefore, careful monitoring of the wound is especially important in the first three post operative months.

Patients with trans-oral maxillectomy had a recurrence rate of 52.1% and those with standard facial incisions had a recurrence rate of 53.3% —an insignificant difference.

The recurrence rate in patients who had a Denker's operation was 30%. These however cannot be compared to the others because they are a

TABLE 7. *Relationship between histological types and prognosis*

Histol type / Prognosis		Squamous cell carcinoma: Cornified	Non cornified	Basal cell carcinoma	Transitional cell carcinoma	Carcinoma simplex	Adenocarcinoma	Total
Within 1 year	Live	3	0	0	0	0	0	3
	Death	9	4	1	0	3	0	17
1–3 years	Live	3	4	0	0	1	1	9
	Death	3	5	0	0	4	1	13
3–5 years	Live	0	6	1	1	1	0	9
	Death	1	1	1	0	0	0	3
Over 5 years	Live	4	3	0	1	0	2	10
	Death	0	0	0	1	0	0	1
Total		23	23	3	3	9	4	65

Fig. 8. Epithelialized wound cavity after the trans-oral maxillectomy.

(f) Post-operative treatment

After local cleansing and packing of the wound cavity a previously prepared temporary dental plastic pélote is inserted. This protects the wound from contamination and from food particles during meals. The permanent palato-dental prosthesis should be applied after about 3 months when the epithelization of the wound surface is completed (Fig. 8).

Pre- and Post-Operative Irradiation

In our earlier cases irradiation was limited to the post-operative application of radium in fractionated doses with a total dose of 4000 mg h. Later we used radium needles (3 mg × 15) in three fractions of one week each arranged against the anterior, posterior and lateral sides of the wound for a total dose of 5400 mg h. The present method of irradiation consists of the pre-operative use of tele-^{60}Co mainly through pendulum irradiation. Total dosage amounts to 3000 rad. The present post-operative irradiation for such pre-operatively irradiated cases is added ^{60}Co 3000 to 4000 rad.

Prognosis

Evaluation of 222 patients one year after radical maxillectomy revealed local recurrence in 115 (51.8%). This was a worse result than we expected. 72.1% of these recurrences were noted within 3 months after surgery.

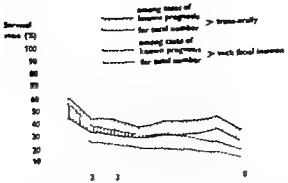


Fig. 9 Survi l ratios f the surgically perated cases f maxillary cancer t the Oto-laryngological Department of Ky h U l ersity duri g 1946–1960

it was apparent that cornification of cells in squamous cell carcinoma does not significantly influence progn i It could clearly be noted however that a better prognosis can be offered in cases of transitional cell carcinoma, basal cell carcin ma, and adenocarcinoma

It is generally conceded that lymphnode metasta is from maxillary can cer is relatively uncommon In our series of 250 cases we found only 71 (27.2%) with palpable submandibular or cervical lymphnodes.

Meticul us histol gical examinati n of 26 specimens removed at radical neck di section revealed positive lymphnodes in only three cases (11.5%)

F r several decades many surgeons have endeavoured to improve the treatment of maxillary cancer Through their eff rts it has become apparent that the most effective treatment is the appropriate combination of irradiati n and urgical excisi n It therefore occurred t us that further inf rmation might be gained by the parallel employment of two different surgical methods, used impartially and compared stringently

The survi al rate of urgically treated cases has been clas ified accord ing t type of procedure employed (Table 8) The one year survival rate for patient with the trans-oral procedure was 60 1% compared to 53.8 in pati nt with tandard facial inci ions. After two years the rate is 42 4% f r trans-oral cases and 37.5% for those with facial inci ion and afte three years was 40.8% nd 33.3% respectively The five-year urvival rat i 39 1 to 29.0 in favor of the trans-oral procedure. With further elapsed time the difference increases, e.g after seven years it is 42.1% and 23.5% in favo of the trans-oral method (Fig 9)

DISCUSSION

I have lready referred to the fact that one can get the same wide exci-si n f tis ue through the trans-oral approach that is possible through anterior faci l incisions. The superiority of thi mode of treatment is verified by the improved prognosi after its use In pite of an often pes-imi tic outlook, it ha long been noted that many patients can be saved

TABLE 8 *Prognosis of the operated cases of maxillary cancer in our Department during 1946–1961 according to operative procedure*

Survival rate (%)

Elapsed year after operation	Operative procedure	Total number	Known prognosis	Number of survival	For total number	Among cases of known prognosis
1	Trans-oral	92	0	11	11.5	00 1
	Facial incision	120	7	13	35.8	53 8
	Denker	10	5	4		80 0
2	Trans-oral	79	59	25	31 [illegible]	42 1
	Facial incision	114	72	27	23.	[illegible]
	Denker	10	5	2		40 0
3	Trans-oral	68	49	20	20 4	40.8
	Facial incision	111	72	21	21 0	33.3
	Denker	9	4	1		[illegible]0
4	Trans-oral	46	34	12	[illegible]0.0	35.3
	Facial incision	114	72	21	18 4	29.4
	Denker	6		1		50.0
5	*Trans-oral*	32	23	[illegible]	28 1	39 1
	Facial incision	103	02	18	17.3	20 0
	Denker	6	2	1		50 0
6	Trans-oral	32	23	9	28.1	39 1
	Facial incision	89	53	14	15	26 4
	Denker	6	2	1		50 0
7	Trans-oral	25	19	[illegible]	32.0	42 1
	Facial incision	77	49	11	14 2	22.5
	Denker	6	2	1		50 0
8	Trans-oral	22	16	5	22.	31.3
	Facial incision	67	[illegible]	7	10 4	16.3
	Denker	6	2	1		50 0

unique and highly selected group and because their number is too small for statistical comparison

Classification of invasion area type was as follows for 115 cases The AIPm group (*Anterior Inferior lateral Posterior Superior medial*) comprised the largest number with a total of 41 cases The Pm group (Posterior Superior medial) was next largest with 22 cases (Table 6) The prognosis is quite different for those patients who had orbital exenteration as opposed to those who did not The mortality for those patients in whom it was necessary to evacuate the orbit was 80 8 compared to 52 7 for patients in whom the orbit was saved

Histopathological re-examination *was done on 65 specimen from patients* in whom the end results were known The findings were divided into four groups according to duration of survival after treatment Consequently

EOSINOPHILIC PAPILLARY CYSTADENOMA OF THE LARYNX

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A case of eosinophilic papillary cystadenoma of the larynx is reported. Its similarity to the salivary gland tumour papillary cystadenoma lymphomatosum (Warthin tumour), syn. adenolymphoma, is pointed out. The reported cases of eosinophilic glandular tumours of the larynx are reviewed, the nomenclature is listed, and the justification of distinguishing them from non-eosinophilic glandular tumours of the larynx is discussed. The occurrence of oncocytes in the normal laryngeal mucosa and in the eosinophilic tumours of the larynx is mentioned.

Benign glandular tumours of the larynx, taken to mean adenomas, cystadenomas, and papillary cystadenomas are extremely rare. So far only about 30 cases are on record, and of these 10 contained eosinophilic glandular epithelium. Non-eosinophilic glandular tumours of the larynx have been described by Moore (1920), Howarth & Chamings (1934), New & Erich (1938), Figi, Rowland & New (1944), Ranger & Thackray (1953) and Stewart (1960). Table 1 lists authors who have described the eosinophilic tumours and the nomenclature which they have used. According to this nomenclature there seems to be a question of a fairly heterogeneous mixture of tumours, but all the cases may be assigned to one of the groups adenoma, cystadenoma, or papillary cystadenoma, and all have contained eosinophilic glandular epithelium. In Heinz' case the tumour contained lymphoid tissue and is designated as an adenolymphoma. This is identical with papillary cystadenoma lymphomatosum or Warthin's tumour, which has not been found in the larynx, neither before nor after. In the 2 cases of Pinkert and & Beck the tumours are described histologically as papillary cystadenomas. This is the justification for including them here, although the heading of their paper says cyst. In Møller and Ørntoft's case the tumour was built up of glandular formation.

In 8 of the 10 cases mention is made of typical oncocytes in the tumours, replacing the normal glandular epithelium partially or entirely, while in 2 cases oncocytes are not mentioned (in Heinz' and Kuhn's cases). Oncocytes are large epithelial cells having eosinophilic granules in the cytoplasm and small pyknotic nuclei. The cells vary in appearance, resembling the organ in which they are found. The word onkos is the Greek for bulky, swollen, and the designation was introduced by Hamperl in 1931. The cells were first described by Schaffer in 1897, but did not have

through the proper use of surgery and irradiation It is of course true that an extensive tissue loss does not guarantee cure

Even with radical surgery I have always felt that preservation of orbital contents is desirable unless extirpation is clearly indicated by invasion of tissue in that area

I am of the opinion that the combined use of irradiation and surgery is superior to either alone This series had post-operative irradiation The results of pre-operative irradiation will become apparent after further observation

ZUSAMMENFASSUNG

Die transorale Maxillektomie erfordert keine Gesichtshautschnittführung und bereitet darum keine Sorgen über postoperative Deformitäten Also erleiden die Patienten fast keine psychische Einflüsse Die Oprationszeit wird bedeutend verkürzt Natürlich kann man damit immer en bloc Oberkieferresektion und auch gleichzeitige Orbitaexenteration ausführen Die Wundenheilung nach der Operation verläuft schnell und sehr günstig Die Fünfjahresüberlebensrate bei den Fällen mit transoraler Methode war 10% höher als dieselbe bei den Fällen mit transkutaner Methode Die otorhinolaryngologische Technik könnte wohl für diese transorale Methode besonders geeignet sein

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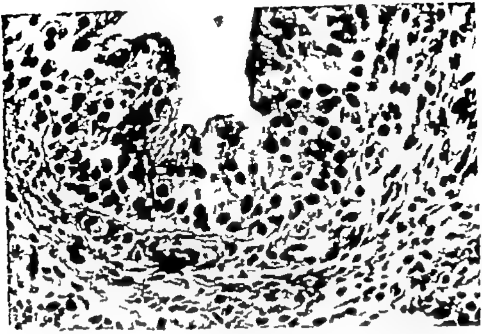

Fig. 2. Area just out ide the cystic w ll w th glandul proliferation. Epithelium f rying thickness. Pronounced i flammation of the stroma.

sented rand mly selected autopsy material. The oncocytes were found in the ex retory ducts and acini of the sero-mucous glands. The glandular cells w re partially replaced by oncocytes, but more disorderly masses of cell w e also f und, indicating ad nomatous growth.

M llic & Ros l (1951) also studying the laryngeal mucosa in a post mortem series, f und the number of oncocytes n the glandular epithelium t increase with ad ancing age. In some of the old persons all glandular epithelial cells were replaced by oncocytes. No oncocytes were found be f puberty.

Gl ndular yst of the larynx are far more comm n than glandular l yngeal tumours. For instance among 722 benign tumours of the larynx N w & Erich 1928) found 33 glandular cysts, but only one glandular tumou an adenom. With some justificati n the glandular cysts may be ncluded among the glandular tumours, a both have arisen primarily in laryngeal gland. Indeed, eo inophilic glandular cyst of the larynx have been reported—a t tal of 3. The first case was described by Nohterl n 1946. The other two were imple retention cyst lined with a simple lumna cystic epithelium composed of oncocytes (Pinkerton & Beck, 1961).

Present Case

A l year-old married watchmaker was dmitted in n acute stat of stridor. During the past 10 years he had been suffering from recurre t attacks f

Fig 1 Th wall of tl cyst tumou Are with a fal ly l w ft n d uble-row pith lium On th l ft a ystic cavit with a taller tratified pithelium Stai ing: Haematoxylin-eosin

n name until 1927 when Zimmermann suggested that they be called pyknocytes because of the pyknotic nucleus These cells have been found in a large number of organs but Nohteri (1946) was the first to find them in the larynx Nohteri made a post mortem study of the laryngeal mucosa in 37 persons aged 0–86 years, 24 being 52 years or over He found oncocytes in 8 all aged 52–86 including 4 over 70 The 37 persons repre-

Table 1

Author	Year	Diagnosis
Som M L and Peimer R	1949	Oncocytic cy taden ma f the l ryn
Heinz, I	1951	Aden lymphoma f th la n
Vosteen K. H	1958	Da oncocyt re Aden m des Kehlk pfes
Ellis, M	1960	Aden ma f th la
Pinkerton P H and Beck, J S	1961	Eosinoph l granula -cell (ocytl) cy t f the lary
Heath, D	1961	Eo i ph l gran la ll t d ma f the laryn
Kuhn, A. J	1961	C stadenoma of the l ry
Capo O A.	1965	O phillcadenom (ncocyt m) f th larynx
Moller J., and Orntoft, I	1965	Lary g al oncocyt ma

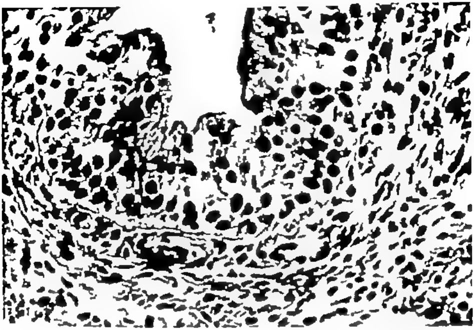

Fig. 2. Area just out ide the cystic w ll w th gland l prolifurati n. Epithelium f arying thickness. Pronounced l fl mm t on of the stroma.

seated a rand mly selected autopsy material. The oncocytes were found in the excretory ducts and cini of the sero-mucous glands. The glandular cells were partially replaced by oncocytes, but more disorderly masses of cell were also found, indicating adenomat us growth.

Mollie & Rossi (1951) also tudying th laryngeal mucosa in a post mortem series, found the number of ncocytes in the gl ndular epithelium t increase with ad ancing age In some of the old persons all glandular epithelial cells were replaced by oncocytes No oncocytes were found before puberty

Glandular cysts of the larynx are far more common than glandular laryngeal tumours For instance amo g 722 benign tumours of the larynx New & Erich (1038) f und 33 glandular cyst but only one glandular tumou n aden ma. With some justific tion the glandular cysts may be included among the glandular tumours, a both have ari en primarily in a laryngeal gland. Indeed, eosin philic glandular cysts of the larynx ha been reported—a total of 3 The first case was described by Nohteri in 1046 The the two we e simple ret nti n cysts lined with a simple columnar cy tic epithel m composed of oncocytes (Pinkerton & Beck, 1961

Present Cas

A 1 year-old married w tchmaker wa admitted in ent state f tridor During the past III years h had been sufferi g from recurrent ttacks of

tonsillitis without laryngeal complications, in particular without hoarseness. One month prior to admission he had developed total aphonia in one day. During the preceding days he had been spraying and painting with cellulose varnish. In the course of some days he developed pain on swallowing and 4 days after the onset of symptoms elevation of temperature to 38.4 C. The temperature had yielded to penicillin for 5 days and his voice was slowly returning, but slight hoarseness persisted until 4 days before admission when the patient caught a cold and then in a few hours, he had lost his voice again. Two days before admission he began running a low-grade fever and on the day before admission his respiration became increasingly stridulous. During the 12 hours prior to admission there had been stridor and cyanosis on the very slightest exertion. The patient had only taken a liquid diet during the past 4 days. Smoking habits 10 cigarettes a day for the past 30 years.

Physical examination revealed total aphonia and mild inspiratory stridor but no cyanosis at rest. Indirect laryngoscopy: the left true cord was completely obscured by a red shiny mucosa-lined well-defined round tumour which appeared to issue from the left false cord. Upon intonation the tumour dipped down into the subglottic space and during this procedure it was seen to be rather larger than a pea and pedunculated. No abnormalities of the vocal cords, the aryepiglottic fold or epiglottis. No peripheral adenitis. Under general anaesthesia a direct laryngoscopy with excision was done. The tumour was removed *in toto* with forceps. During this procedure it ruptured and a few drops of yellow secretion were evacuated from its base.

There were no postoperative complications and the patient was discharged on the 5th day. At that time his voice was almost normal and the only abnormal laryngoscopic finding was a little reddening anteriorly on the left false cord.

During his stay in hospital bilateral nephrolithiasis and mild diabetes mellitus were diagnosed. The thyroid gland was normal to palpation and the serum calcium was 9.1 mg/100 ml. Haemoglobin 10_%. E.S.R. 10 mm/hour, white cell and differential counts normal.

At a follow-up admission 2 months later his voice was normal and no abnormalities were found on laryngoscopy or on tomography of the larynx.

Microscopically the tumour consisted of a fairly large folded somewhat branched cavity lined predominantly with a double row of columnar cells. In a few places the epithelium had proliferated and become stratified. The cavity contained a deeply indented structure lined with epithelium of the same kind. There was fairly marked eosinophilia of the cystic and papillary epithelium. The nuclei were in many sites small and pyknotic. Where the epithelium was distinctly made up of a double row the nuclei were situated basally in the luminal row of cells. The pedicle of the papilloma was delicately branched consisting of loose collagen connective tissue. Outside the cystic cavity there were a few glandular components lined with the same type of epithelium but with more pronounced proliferation. The cells were partly columnar and partly polygonal with the nuclei situated centrally and in some places with a finely granular cytoplasm. The entire prominence was the seat of rather severe inflammation with granulocyte and round cell infiltration in places with the formation of small abscesses. There were only a few and scattered lymphocytes and no lymphoid tissue. No histologic criteria of malignancy. The tumour was composed as a papillary cystadenoma lymphomatosum (Warthin's tumour).

Fig. 1. Glandular epithelium i higher magnification. The l minal cell contain eosinophilic granules.

without lymphoid tissue Histological diagnosis cystopapilloma f the larynx with secondary inflammat on

DISCUSSION

It is evident from the histological description of the present case that the tumou was built up as a papillary cystadenoma and may therefore be cla sified as a glandular tumour of the larynx. It differs from a simple retention cyst in ha ing an epithelium with papillary excrescences, while in a lenti n y t it is usually simple and often flattened The areas of glandular prolif ration just outside the cystic wall are not seen in reten tion cyst which are in most cases unilocular and surrounded with normal gla dular ini and excret ry ducts Since, as already mentioned, 3 cases of eosin philic ret nti n cysts are on record th eosinophilia of the present tum ur cannot be used as a differential diagnostic criterion again t a retention cyst

Th d fferential diagnosis from laryngopyocele ought to be mentioned, a n th course of th exci l n a few drops of yellow secretion, which m ght be p s, we e seen at its base and a the hi tological examination showed m ll abscesses. However considerably larger quantities of pus, nd palpabl welling on the neck (Glatz, 1961) mu t be demanded for a diagnosi f a full-blown laryngopyocele

As far as the eosinophilic cells are concerned some must be assumed to be typical oncocytes, but this does not by any means apply to them all. This finding accords very well with those of some previous authors. There are several concise descriptions of an even transition, in the same preparation, from normal epithelial cells without eosinophilia, by way of epithelial cells without eosinophilia by way of epithelial cells with slight eosinophilia and finely granular cytoplasm to typical oncocytes with marked eosinophilia, coarse granules, pyknotic nuclei, and swollen cytoplasm. The shape of the oncocytes in the reported cases ranges from flattened by way of polygonal to tall columnar. According to some authors the nuclei are central while others have reported eccentric nuclei usually at the luminal end of the columnar cells. In some cases the cell limits are stated to be distinct while in others they are reported to be ill-defined.

According to what has been stated above it would seem to the author that the eosinophilic cells, including the "typical" oncocytes are in many cases so polymorphous that it is impossible to decide with certainty whether the eosinophilic cells are variants of the typical oncocytes, "immature" oncocytes, or entirely unrelated to oncocytes.

The problem is known from the parotid tumour papillary cystadenoma lymphomatosum (Warthin's tumour). This tumour is built up exactly like the above-mentioned papillary cystadenomas, including the present case, except for the fact that the parotid tumour includes lymphoid tissue. This was pointed out by Kuhn in 1961. In Warthin's tumour there is a columnar epithelium consisting of eosinophilic cells, usually arranged in two rows, and there has been a great deal of discussion as to whether these cells have anything to do with oncocytes. Eneroth (1964), among others, has called attention to the similarity between oncocytes and the cells in Warthin's tumour, especially those of the inner row, in sites where the epithelium is distinctly arranged in two rows. In 1962 Cläser definitely demonstrated oncocytic structures in Warthin's tumour, and Lehnhardt & Fischer in 1961 found typical oncocytes among the eosinophilic cells in Warthin's tumour.

Jaffé (1932) introduced the term oncocytoma for the parotid tumour papillary cystadenoma lymphomatosum, but to-day most authors (Ackermann 1943, Hevenor & Clark 1950, Cläser 1962, Hantschmann & Jaquet 1963, Eneroth 1964) agree with Hamperl who in 1962 clearly pointed out that the term parotid oncocytoma was to be reserved for a tumour which is exclusively or predominantly made up of oncocytes. The present author suggests that in analogy the term laryngeal oncocytoma be reserved for a tumour which is made up exclusively or predominantly of oncocytes.

As mentioned above Nohteri (1946), in a randomly selected post mortem series, found oncocytes in the larynx of one-third of all persons over 52 years of age and in none under 52. It is remarkable also that all 11 cases of eosinophilic laryngeal tumours, *including the present case*, have oc-

curred in patients over 50 The non-eosinophilic glandular tumours are found in patients who are on the average somewhat younger

The symptoms and signs of the eosinophilic tumours do not permit a distinction of eosinophilic from non-eosinophilic, as hoarseness is the sign which i most commonly found, and hoarseness is present in 95% of all benign tumours of the larynx (New & Erich, 1938)

In their ites of predilection the eosinophilic tumours also do not differ from the ther glandular tumours. They occur where the concentration of sero-mucous glands is at a maximum, viz. in the ventricles and around the false and true cords.

Data concerning surgical procedures and follow u studies are sparse but in one case there was a definite recurrence (Som & I elmer 1949) Six weeks after th removal of the tu nour the larynx was almost packed with tumour ma ses. These masses had to be removed by laryngofissure and there was no further recurrence for 18 months. In Heath s case a non-eosinophil c cystadenoma ha l been removed 17 months before the removal f the eosinophilic cystadenoma.

CONCLUSION

The nomenclature rel ting to the benign glandular tumours of the larynx, especially of the eo inophilic ones, is very heterogeneous, but so far it has been pos ible to classify all cases in one of the groups adenoma, cyst adenoma, papillary cystadenoma In the present author s opinion this nomenclature is applicable. It may then be supplemented by "eosinophilic" oncocytic or lymphomatosum" according to whether the glandular epithelium is eosin philic, particularly rich in oncocytes, or the tumour contain lymphoid tissue The number of reported cases is still too small for a deci i n as t whether it i justified to distinguish the group eosinophil glandular tumours of the larynx a a separate entity in particular whether it i ju tified to di tinguish it from the other glandular tumours

ACKNOWLEDGMENTS

The uthor i ndebted to Professor Steen Olsen and to Dr T Homm lgaard for th ir interest and h lpf l ess.

ZUSAMMENFASSUNG

Ein F ll nes eosinophilen pap illären Zystadenoms im Larynx wird be prochen Ei Äh lichk it mit dem Spei h ldrüsentumor d. h dem papillären Z stadenolymphom (Warthin) oder Adenolymphom, ist erw äh t. Bisher er ffentl hte F lle ler eosi ophilen gla dularen Laryn t moren sind zusammen gef st, die erschiedenen N menklaturen sind genannt und die Berechtigung der Tren ung on den n hteosinophilen Laryn tumoren wird disk tiert. Über das Vorkommen der Onkozyten in der normalen Laryn mucosa sowie i eosinophilen Lary tumoren wird bericht t.

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PATHOLOGICAL AND FUNCTIONAL CHANGES FOLLOWING HEMISECTION OF THE LATERAL AMPULLARY NERVE

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An attempt was made to section the canalicular branch of the lateral ampullary nerve in the cat. In successful cases the section was associated with degeneration of both sensory and marginal epithelium and the stroma. The animals showed signs of an acute vestibular disorder consisting of disequilibrium, spontaneous nystagmus toward the unoperated ear, type III positional nystagmus, perverted nystagmus in response to caloric irrigation on the operated side and a directional preponderance toward the unoperated ear during optokinetic, caloric and rotatory tests. Section of superior and or lateral ampullary nerves to a certain extent mimicked the clinical signs of a labyrinthectomy. The clinical implications of the vestibular disorder associated with damage localized to the crista ampullaris is discussed.

The fibers innervating the sensory epithelium of the crista ampullaris form two branches, one from the canalicular side and the other from the utricular side (Ramón y Cajal, 1909–1911; Lorente de Nó, 1926). Classed on the basis of diameter three types of nerve fibers may be found in each branch. The large size innervates three to five hair cells at the summit of the sensory epithelium. Within the crista there are no large fibers crossing either from the utricular to the canalicular side or vice-versa. The middle size fiber is predominantly found in the lateral parts innervating many cells. These fibers present numerous collaterals forming an intra-epithelial plexus on each side of the crista. Apparently there is no crossing of fibers or collaterals from one side to the other. The smallest fiber is found at the base of the sensory epithelium innervating numerous hair cells. Its collaterals form another intra-epithelial plexus extending along the base and interconnecting the sensory cells of both sides. The interconnection takes place in the lateral areas of the crista. The nerve endings of the crossed collaterals is unknown. The functional significance of this distribution of nerve fibers in the crista is a matter of speculation.

The question was raised whether changes in vestibular reflexes could be associated with section of either the canalicular or utricular branch of an ampullary nerve. For this purpose the lateral ampullary nerve of

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the cat could be suitable because the fibers emerging from either the canicular or utricular side are distinctly separated and suitable for independent sectioning.

The purpose of the experiment reported here was to study the changes in vestibular reflexes associated with section of either the canalicular or utricular branch of the lateral ampullary nerve in the cat. It was assumed that the hemisection, for instance sectioning the utricular branch, would result in degeneration of all its fibers including the collaterals crossing to the canalicular side. If the operation produced no alteration of the vascular supply, then all the sensory epithelium, the innervation of the canalicular side including its crossed collaterals, and the stroma of the crista would be preserved. A successful preparation could be of some importance for the understanding of the neural mechanism underlying the reflexes elicited by stimulation of the horizontal semicircular canal. For comparison purposes, other vestibular lesions were included in the design of the experiment, that is, complete section of either the lateral or superior ampullary nerves and complete section of both.

METHODS

Preparation and testing

Healthy adult cats between 2 and 4 kg were anesthetized with intraperitoneal Pentobarbital Sodium (Diabutal 60 mg/ml) using a dosage of 0.6 ml/kg body weight. The ears were examined with the Zeiss operating microscope and animals with infected external auditory canals or abnormal tympanic membranes were rejected. For the recording of eye movements, button electrodes were inserted in the malar bones and the glabella. The upper canines were drilled close to the gingival margin for the insertion of a wire in order to fix the head in the testing box as described by Henriksson, Fernández & Kohut (1961). All general anesthetics were covered with an intramuscular injection of Bicillin (1.2 million units).

After the elapse of at least one week, each animal was tested according to the procedure used throughout the experiment. Posture, locomotion, hopping, placing and jumping were observed; righting reflexes with and without vision during free fall were tested and muscle tonus assessed. The animal was then securely fixed in the testing box and eye movements in erect, right lateral, supine and left lateral positions were directly observed and simultaneously recorded on an electronystagmograph. The test was then repeated with the animal in total darkness. The positional nystagmus resulting from these tests were classified according to the nomenclature proposed by Nylén (1950). Optokinetic responses were tested by projecting on a concave screen a film of alternate black and white lines moving at a speed of 24 degrees [illegible]. For the rotatory test the animal was positioned on the rotating platform so that the horizontal canal was in the horizontal plane. The platform was accelerated at 2.5 degrees [illegible] until it

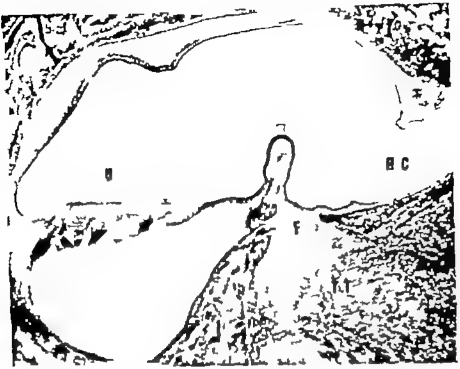

Fig. 1 Photomicrograph showing the fenestra for approaching the horizontal ampullary nerve. *U*, utriculus. *HC*, horizontal semicircular canal. *F*, fenestration at the level of the lateral ampullary nerve. *TT*, tensor tympani. Marker 1.6 mm. Hematoxylin-eosin stain.

reached an angular velocity of 180 degrees/sec. This velocity was maintained for 80 seconds and then the platform was decelerated at 25 degrees/sec². Rotation was performed in clockwise and counterclockwise directions. The caloric test was done with the animal placed on a stand arranged so that the horizontal canal was in the vertical plane, ampulla uppermost. The ears were irrigated with thermostatically controlled water at 28 and 48 C, 5 C being used when the responses were equivocal. Irrigation was for a period of forty seconds and the lights were switched off immediately upon the termination of irrigation; all eye movements were recorded with the animal in total darkness. Any animal with a preoperative abnormal response was excluded from the experiment.

Surgical technique

The approach for section of the ampullary nerve was a modification of that described by Fernández, Alzate & Lindsay (1959). Under Diabutal anesthesia and with strict asepsis, a suprameatal approach was made and the outer attic wall drilled down. The incus and head of the malleus were removed and the tensor tympani freed and displaced into the hypotympanum. From this stage onwards the operative site was continuously ir-

rigated with mammalian Ringer's solution The tympanic portion of the facial nerve was exposed and sectioned to facilitate the approach A fenestra was created between the ampullae of the horizontal and superior canals thus exposing the corresponding ampullary nerves and visualizing the canalicular and utricular branches of the horizontal nerve For surgical access to the superior ampullary nerve the fenestra was enlarged anteriorly and superiorly in order to fully expose that structure Section and/or hemisection was performed with a fine needle the tensor tympani swung over to occlude the fenestra and the incision closed in layers The microscopic appearance of the fenestra after 15 days is shown in Fig 1

The animals were examined clinically and positional testing performed on alternate postoperative days In addition optokinetic, rotatory and caloric tests were carried out on the fifth day postoperatively and, thereafter at intervals of approximately ten days until the animals were sacrificed This interval was chosen in order to diminish or avoid habituation of responses Most animals were sacrificed between the fifteenth and twenty fifth days, but a few were observed for one week or less and a similar number kept for varying periods up to the fiftieth postoperative day

The animals were perfused by the standard intravital method of fixation 10% formalin being used in a few and Heidenhein Susa in the majority The hind brain and temporal bones were removed in one block and prepared for histology Serial sections were stained with Hematoxylin eosin Mallory and Weil techniques In four animals, counts of the hair-cell population of the horizontal crista were made in order to assess the extent and distribution of the lesion In these animals all sections containing the horizontal crista were stained and counts made independently of the canalicular and utricular slopes Each section was counted four times by one of the authors and the average of the results taken The hair-cell populations were then expressed as a total of the numbers thus obtained For purposes of comparison this procedure was repeated in two unoperated horizontal cristae This method of counting is inaccurate in that one cell may appear in consecutive sections and thus be counted twice The result obtained can therefore be regarded as only an approximation but this does not affect the comparative value of the method

RESULTS

Thirty three animals were operated on but three died within the first two postoperative days In the remaining thirty the following operations were performed controls, section of lateral ampullary nerve section of superior ampullary nerve combined section of lateral and superior ampullary nerves, and hemisection of the lateral ampullary nerve Early in the course of the experiment it became evident that there was variability in the behaviour and responses of animals with supposedly identical lesion Subsequent histological examination confirmed that the extent of the

damage produced was in many cases greater than had been intended, particularly so in the group of attempted hemisections. Thirteen of the thirty were found to have either partial lesions of both the horizontal and superior cristae of varying degrees or else massive middle ear infections with resultant clinical deterioration. These animals were therefore excluded from the reported results and only those with well-defined lesions will be described (17 cases).

A. *Control*

The controls (4 animals) are animals in which a labyrinthine fenestration was performed as described above but the ampullary nerves were not damaged surgically. Clinical evidence of a slight disorder of equilibrium (disturbances of posture and locomotion) was observed for three days following surgery. One animal exhibited spontaneous nystagmus toward the unoperated ear on the first postoperative day, probably due to incomplete recovery from anesthesia. No spontaneous nystagmus was detected in the other three animals. A mild irregular positional nystagmus was recorded for a few days in three cats. The optokinetic, rotatory and caloric responses revealed no abnormality. The histological picture of the vestibular receptors in the operated side was indistinguishable from that of the unoperated ear.

B. *Sections*

Section of lateral ampullar nerve (three animals)

The animals presented clinical signs of unilateral vestibular disorder consisting of disequilibrium, spontaneous and positional nystagmus, and canal paralysis of the operated ear. The disturbance of equilibrium was shown by an unsteady gait, asymmetric posture of the head, and lateral pulsion toward the operated side. These disturbances improved progressively so that at about the twentieth day little abnormality could be detected. The righting during free fall, however, did not recover to that of the skillful turning of the normal cat. A spontaneous nystagmus toward the unoperated ear was seen for about three days but it was recorded in total darkness until the tenth to fifteenth postoperative day. When the animal was placed in the supine position or with the unoperated ear undermost, the nystagmus exhibited a rotatory component and its rhythm became faster, irregular or fibrillatory; distress was shown by vocalization and struggling. After disappearance of the spontaneous nystagmus, the postural test still produced a direction fixed positional nystagmus which subsided progressively until complete disappearance within a few more days.

The eye movements elicited toward the side of the lesion by optokinetic and rotatory tests were greatly reduced in amplitude and frequency, while those produced toward the unoperated ear were enhanced. No caloric reaction

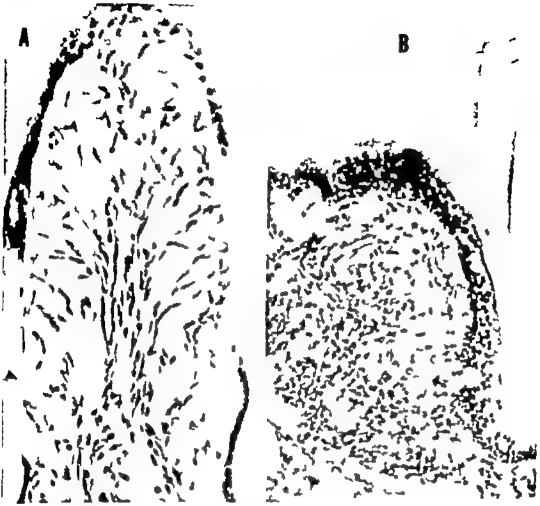

FIG 2 Complet secti n f lateral amp ll ry n rv 4 crista mpullari lateralis howing necrosis of both sen ry a d margi al pith li m and troma B, cri ta mpullari superi f tl e same animal h wi g n abn rmalities Marker 180 μ Hem t xylin eo in tal

could be demonstrated in the operated ear even with o C irrigation The caloric test in the unoperated ear showed a significant difference between cold and hot reactions The nystagmic responses of the former were depressed while those of the latter exhibited a clear cut enhancement As expected these asymmetric responses were compensated in time

The histological picture of the crista ampullaris lateralis (Fig 2 A) showed necrosis of both sen ory and basal epithelium The cupula was detached and displaced towards either the canal or utriculus The crista was covered by a low cuboidal repairing epithelium The empty appearance of the crista s matrix was a characteristic feature of these and other complete sections of ampullary nerves No abnormality was f un l in the crista of the superior canal (Fig 2 B) or other vestibular recept rs

Section of superior ampullary nerve (one animal)

A complete section of the superior ampullary nerve with a histological damage of the crista ampullaris lateralis was never produced Fig 3 B

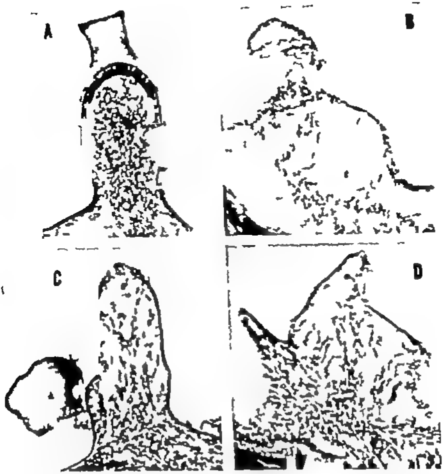

Fig. 3. Section of superior ampull ry ers associ ted with ecrosi f the crista sho B, nd slight cell dege eratio of sensory ep theli m f crista mpullari lateralis how i A Complet section of both horizo tal nd perior mpullary nerves resulted i necrosis f correspondi g mpullae how i C nd D Notice detachment of cupula i C M rker 200 Hem t xyl n-eosi stain.

show the necrosis f the cri ta of the superio canal, and Fig. 3 A demonstrates that there wa a light but definite symmetrical diminution in the number of sensory hai cells of the crista ampullaris lateralis. Despite the minimal degree f hi t logical damage to the latter its caloric responses were depressed

Section of both uperi r and l teral ampullary nerves (thr anim ls)

F g 3 C nd 3 D dem n trate necrosi of both cristae after sectioning their respecti e nerves. The necrosi involved both sensory and basal pith lium d troma. No pathological changes were found in other estibular receptors. This group exhibited persistent sign of unilateral labyrinthine los t the twenty fifth postoperati e day There was slight

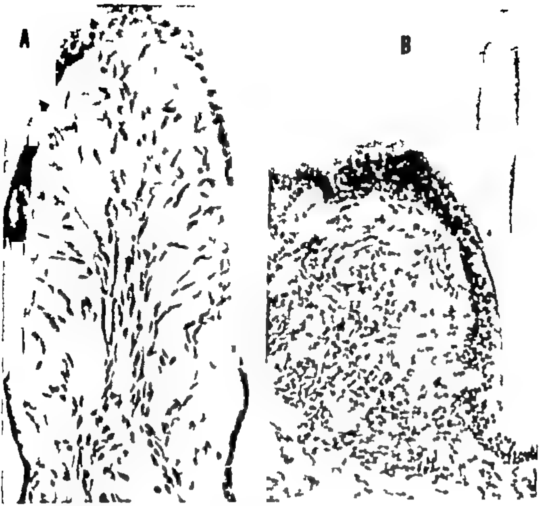

Fig 2. Complete ection f lateral ampullary nerve (l ta ampullari lat rali howl g necrosi of both sensory and margi l epitl lium nd troma B, cri ta mpullari superi r of the sam nim l h wing no ab rmalities Mark 180 ; Hematox lia eo l tain

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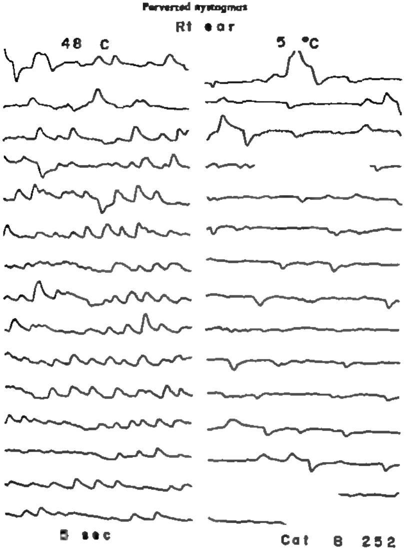

Fig. 5. Perverted nystagmus elicited by irrigation of right ear with water at 48 and 5 C. In this and following electronystagmographs the records must be read as continuous recording from top to bottom and from end of irrigation (40 seconds) until nystagmus disappeared.

clinical disturbance of equilibrium for four or five days after the operation. Spontaneous nystagmus toward the unoperated side was seen for two to three days but it was recorded in total darkness for a longer time (14 days in one animal). The positional test gave a characteristic type III positional nystagmus, that is, it sometimes was direction fixed, at other times was direction-changing, and occasionally, as shown in Fig. 4, the nystagmus changed its direction during a given head position. In general, the positional nystagmus was a persistent type, reproducible non-par

Positional nystagmus

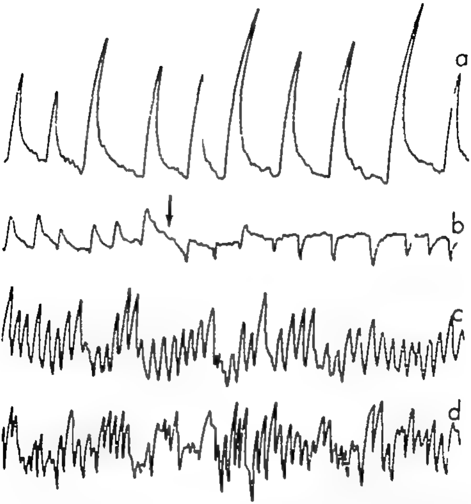

FIG. 4. Positional nystagmus taken in total darkness after hemisection of the right ampullary nerve. In this and following electronystagmographs an upward deflection indicates a jerk toward the left while downward deflection means a jerk toward the right. *a*, spontaneous nystagmus. *b*, right lateral position producing a change in direction of nystagmus at the point indicated by the arrow. *c*, supine position resulting in significant increase of frequency. *d*, left lateral position in which the nystagmus became dysrhythmic. Marker 5 seconds.

head rotation to the side of the lesion, a broad based stance and some hind-limb ataxia. The righting reflex during the free fall was absent in the right lateral position, i.e., with the operated ear undermost. A spontaneous nystagmus to the unoperated ear was present initially and a type II direction fixed positional nystagmus (toward the unoperated ear) was still present at the twenty fifth post-operative day in the supine position. Caloric testing produced no response from the operated ear while in the unoperated side there was a clear-cut preponderance of hot over cold responses.

C. Hemisection

Section of the canalicular branch of the lateral ampullary nerve was done in thirteen animals. As explained above the results were inconsistent but a group of five animals exhibited similar responses. These had a slight

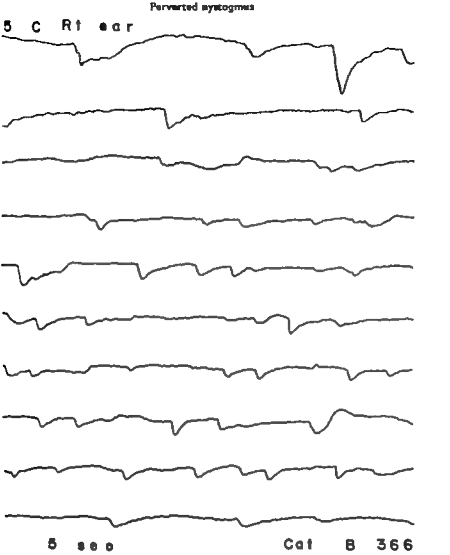

Fig. 7. Cat B-366. Perverted nystagmus elicited by irrigation of right ear with water at 5 C.

operative day. Subsequently the animal developed a respiratory tract infection and had to be sacrificed fourteen days after surgery. At that time spontaneous nystagmus toward the unoperated ear was present in the dark and only a reduced perverted response was obtained on caloric testing. The lesion produced in this animal, unlike the other three, was therefore of a progressive nature and the histological appearance shown in Fig. 8 may not represent the state of the crista on the fifth post-operative day when the perverted response was obtained.

The fifth animal which is still alive exhibited a perverted nystagmus

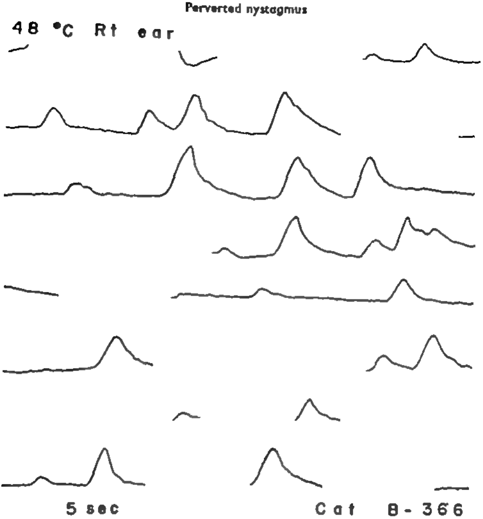

FIG. 6 Cat B-366 Perverted nystagmus elicited by irrigation of right ear with water at 48 C.

oxysmal but occasionally would become dysrhythmic or fibrillatory. Its intensity increased in the supine position and when the unoperated ear was undermost; sometimes a rotatory component was observed.

The nystagmic responses to optokinetic and rotatory stimulation exhibited a preponderance of that nystagmus elicited toward the unoperated ear. The caloric test produced unexpected results. Irrigation of the operated ear with cold water resulted in an ipsilateral nystagmus while hot irrigation produced a nystagmus to the contralateral side. Representative records of this perverted caloric response from two of these animals are illustrated in Figs 5, 6 and 7. In cat B-292 (Fig 5) calorization of the right ear (the operated ear) with 48 C water should have produced nystagmus toward the right which, with our instrument, would be recorded as a downward deflexion. As shown in the figure the deflexion was upward, indicating nystagmus toward the left. Irrigation of the right ear with water at 5 C also produced perverted nystagmus. The perverted responses of the animal B-366 illustrated in Figs 6 and 7 were obtained on the fifth post

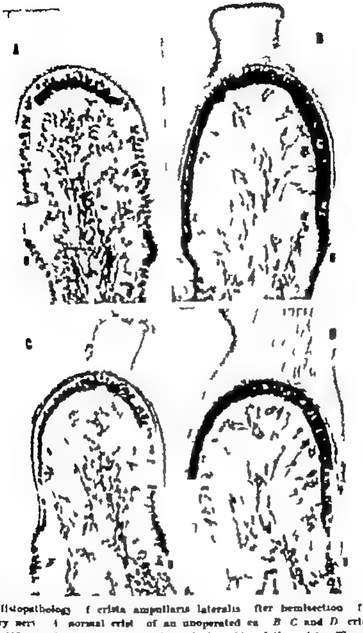

Fig. 9 Histopathology of crista ampullaris lateralis after hemisection of the lateral ampullary nerve. A normal crista of an unoperated cat. *B*, *C* and *D* cristae of Cat B-143, B-351, and B-319 respectively. U: utricular side of the crista. The degeneration of stroma and both sensory and marginal epithelium is evident. Marker 200 μ. Hematoxylin-eosin stain.

utricular slope the marginal cells appeared healthy, the sensory epithelium was of greater depth and the hair cells, although reduced in number, were several times more numerous than on the canalicular side. As shown in Table 1 the hair cell counts demonstrated the asymmetry and degree of the lesion as compared to the controls. The controls exhibited an asym-

Fig. 8. Cat B 366. Crista ampullaris lateralis after hemisection of lateral ampullary nerve. *A*, Weil stain; *B*, hematoxylin-eosin stain. Note necrosis of sensory epithelium on the canalicular side and partial detachment of the cupula. Round degenerated cells are seen on the surface of and within the crista and in the endolymphatic space. Magn. × 200.

at the thirtieth post-operative day. The nystagmus was recorded in total darkness and directly observed with an infra red viewer. The direct observation confirmed the electronystagmographic recording of a perverted purely horizontal nystagmus.

In these five animals, the responses of the unoperated ear to caloric stimulation showed a directional preponderance of hot over cold irrigations. That is both the intensity and duration of nystagmus elicited towards the unoperated ear was larger than that elicited toward the operated side.

The histological pictures of the cristae ampullaris lateralis of the four *sacrificed* cats with perverted nystagmus are shown in Fig. 8 and 9. The appearances were consistent from one animal to another. On the canalicular slope there was either necrosis of the sensory epithelium (Fig. 8) or a severe loss of sensory, supporting and marginal cells (Fig. 9). On the

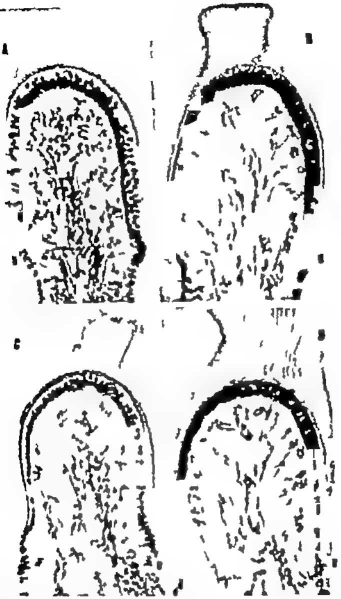

Fig. 9 Histopathology of cristae ampullaris lateralis after hemisection of the lateral ampullary nerve. *A*, normal crista of unoperated ear. *B*, *C* and *D* cristae of Cat B-182, B-252, and B-319 respectively. *U* utricular side of the crista. The degeneration of stroma and both sensory and marginal epithelium is evident. Marker 200 µ. Hematoxylin-eosin stain.

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TABLE 1 *Population of sensory hair cells on the canalicular and utricular side of the crista ampullaris lateralis of four animals with perverted nystagmus*

The counting was done four times in each animal Numbers represent averages of the four counts In two animals (B-182 and B-319) the unoperated ear was used as control

	Hemisection		Control	
	Canalicular side	Utricular side	Canalicular side	Utricular side
B-306	0	450		
B-252	116	881		
B-182	63	822	2873	2581
B-319	104	11 6	2851	2596

metry in the sensory cell population i e., the canalicular side of the crista ampullaris lateralis had about ten per cent more sensory cells than the utricular side There is no evidence that this normal asymmetry is functionally significant In the experimental animals there was an obvious loss in the total number of sensory cells the loss being predominantly larger on the canalicular side that is, on the side of the hemisection

Involvement of the crista s stroma was a prominent feature as illustrated in Figs 8 and 9 by the empty appearance of the core The involvement was severe on the canalicular side and moderate on the other Our histological methods are inadequate for revealing details of nerve degeneration thus there is some uncertainty regarding the question whether all fibers of the canalicular side were sectioned and whether some fibers from the utricular side were encroached upon by the lesion The serial sections stained with various methods however revealed no retrograde degeneration in Scarpa s ganglion

D Other Histological Findings

The histological appearance of the cupula seemed to depend on the extension of damage to the sensory epithelium In those cases of necrosis of all the sensory hair cells the cupula was detached from the crista (Fig 3 C) Apparently there was no absorption or degeneration of the cupular substance at least for a period of about one month Partial necrosis as shown in Fig 8 produced partial detachment while degeneration of some cells (Fig 9) may be associated with some changes in position of the cupula None of the animals in the reported series showed any histological abnormality of utriculus, sacculus or posterior ampulla

Half of the reported cases showed varying degrees of outer hair cell degeneration in the basal coil of Corti s organ on the operated side (Fig 10) This could not be correlated with the type of lesion produced presence of blood or precipitate in the perilymph or infection in the bulla Pre-

FIG. 10 Degenerative processes i the org of Corti of variou im ls. 1 organ of Corti with no abnormalities. The photomicrographs from 2 t 6 were rra ged i order from severe t slight hair cell loss. Each phot micrograph correspond to different nimal. Marker 100 μ. Hemat xylin-eosin stai

sumably ibrational trauma from the electric drill was responsible for thi finding

N abnormalities were found in Scarpa s ganglion, brainstem, cerebellum meninges in any of the animals The section of the facial nerve was a sociated with Wallerian degeneration of the distal stump followed by a distl et proliferation of Schwann cells forming a neuroma. The proximal stump sh wed regeneration f fibers interwoven with the neuroma

COMMENTARY

The hi t l gy demon trated that the purpose of this experiment was n t ttained Firstly the urgical procedure permitted the section of the canali ular branch of the lateral ampull ry nerve without encroaching upon th utric lar bran h, but the opposite condition was not possible Sec ndly the hemisection w a sociated with extensive degenerative changes in the epith lium and stroma f the crista In our opinion the ause of these degenerativ changes wa an ischemic necrosis produced by urgical trauma During the sectioning of the canalicular branch, the bl od vessel running n the surfa of that branch w re observed to

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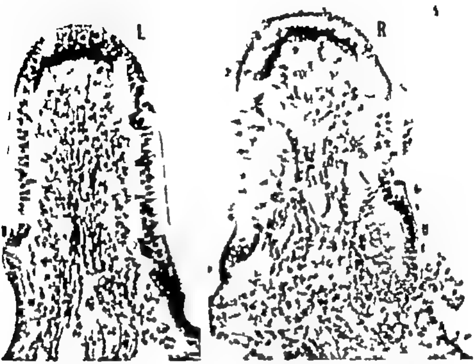

FIG. 11 Left (*L*) nd Right (*R*) crista mpull e lateralI f cat D-282, [utricul ide of the crist The hemisectio f l teral mpullary nerv w done i the right side nd the nimal w sacrificed t th third post perati day Acut m g f cell degenera tion i sensory d marginal epitheli m and trom n es dent Notice pat ncy of blood essels. M ker 200 Hemat li eosi st in.

degree and ext n ion of the lesi n, number and class of receptors in volved, te

All th animals reported here with a lesi n of the vestibular sense organ hav both pontaneous and positi n l nystagmus. There is no dif ficulty i differentiating a directi n-changing r an irregular or a par xy mal nystagmu fron a spontaneous nystagmus, but it is not ea y t diff renti te between a direction-fixed type and a spontaneous nystag mu exacerbated by posture When the pontaneous nystagmus disappears, then th questi n arises s to whether the disorder seen and recorded is a tru positi nal ny t gmu f type II r l a latent spontaneous nystagmus leased by pos ti nal timulati n.

Th observ tion on c lori responses raised once m re the question r g rding the natomical rigin in the sense organs of canal paresis and directi n l [rep n lerance f c lori nystagmu s d fined by Fitzgerald & H llp k (1942 nd Cawthorne Fitzgerald & Hallpike (1942) Th y postul ted that in man lesi n localized to the crista ampullari laterali result i n l paresi while a utricular lesion produces directional pre-

collapse, producing blanching of the utricular nerve. The acute stage of such a vascular disturbance was illustrated by an animal sacrificed three days after hemisection. The cat exhibited strong disorders of posture and motor performances, paralytic spontaneous nystagmus and an absence of caloric responses in the operated ear. The histological preparations showed necrosis of most of the sensory hair cells of the crista ampullaris lateralis with preservation of their supporting cells (Fig. 11). The cupula was detached and numerous degenerated cells were found in the stroma and in the endolymph around the crista. The vascular disturbance must have been transitory since in this animal and all others reported here the blood vessels of the crista were patent. Apparently the circulation was restored through collaterals. It is possible that in man a similar vascular disturbance might result in permanent damage to the sense organs. If circulation is re-established then the histopathological interpretation of a vascular accident might become a very difficult decision.

Perhaps the most striking feature associated with hemisection of the lateral ampullary nerve was the perverted nystagmus elicited by caloric stimulation of the operated ear. The neural mechanism underlying the perversion of this reflex is unknown. The possibilities that it represented a latent or provoked nystagmus or might have represented the response of the vertical canals were discarded. We assumed that the disorder was associated with factors such as partial damage of the sensory epithelium and asymmetry of the lesion. Perhaps the partial detachment of the cupula produced a derangement of the cupular mechanism resulting in a perversion of the sensory coding.

Perverted nystagmus has been found in certain lesions involving the brain stem of man (Jones, 1918; Shuster, 1933; Spiegel & Sommer, 1944; Fisher, 1956; Riesco-MacClure & Martinez, 1957) and animals (Maxbaum, 1938; Buchanan, 1940; Cranmer, 1951; Fredrickson & Fernandez, 1964). It has been considered an important sign for diagnosis of localization in that it has been found associated with certain lesions encroaching on the vestibular nuclei. Perverted nystagmus, however, may occur in certain peripheral lesions of both experimental animals as shown here or in man as postulated by Klestadt (1930). The results show once more that abnormal eye movements may help but are not a pathognomonic sign in the diagnosis of localization.

The type III positional nystagmus is another sign often associated with diseases of the central nervous system. The results of our investigation indicates that peripheral lesions localized in the crista ampullaris lateralis and perhaps in any vestibular receptor may produce a type III or any other positional nystagmus. In agreement with Lindsay & Hemenway (1956) this and other types of positional nystagmus of peripheral origin seem to be the result of an asymmetry in the sensory input caused by unilateral sudden partial loss of vestibular function. Apparently the type of nystagmus, at least in animals, is determined by many factors such as

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ponderance a combined canal paresis and directional preponderance was associated with a combined canalicular and utricular lesion In the animals of our series the hypothesis holds only to a certain extent The cases of hemisection had a directional preponderance toward the unoperated ear which according to the hypothesis, indicates a utricular lesion of the operated side Yet the studies of complete serial sections failed to demonstrate a histological difference between the sensory epithelium of right and left utriculus The cases of complete necrosis of the crista ampullaris lateralis exhibited as is implicit in the hypothesis, a canal paralysis, but again the animals had an enhancement toward the unoperated ear As in previous cases no histological abnormalities were found in the utricular sensory epithelium of either side The experimental evidence at least in the cat indicates that canal paresis or paralysis combined with directional preponderance may occur in lesions localized to the crista ampullaris lateralis Although in man there is no evidence demonstrating a correlation between directional preponderance and a unique utricular lesion it is possible that differences in order from cat to man may cause differences in behavior of abnormal vestibular sense organs. Perhaps the set of assumptions including the most recent ones (Carmichael Dix & Hallpike 1965 Hallpike 1965) for explaining the neural mechanism underlying canal paresis and directional preponderance are applicable only to man At any rate the assumption that the tonus elements are subserved by the utriculus is at variance with the electrophysiological evidence that the utriculus and semicircular canals have resting activity (Löwenstein 1950) Apparently the contribution of the vestibular system to the muscle tone is the result of the summation of this resting activity As a matter of fact the excitation or inhibition of the resting activity of one lateral semicircular canal produces a profound tonus imbalance as demonstrated by conjugate deviation of the arms and eyes (slow component) and lateral pulsion of the body In our opinion tonus imbalance in mammals may result from a lesion localized to any vestibular receptor

ZUSAMMENFASSUNG

Es wurde versucht den kanalseitigen Teil des Nervus ampullaris lateralis der Katze durchzuschneiden In erfolgreichen Fällen zeigte die Sektion eine Degenerierung des sensorischen und marginalen Epitheliums und des Stromas. Die Tiere zeigten eine akute vestibuläre Störung bestehend aus gestörtem Gleichgewicht spontanem Nystagmus zu dem nicht operierten Ohre Typ III Lagenystagmus, pervertiertem Nystagmus nach Wärmespülung der operierten Seite und einer Nystagmusbereitschaft zu dem nicht operierten Ohre im optokinetischen und kalorischen Tests und im Drehtest Das Durchschneiden der Nervi ampullaris superior und/oder lateralis liess zu einem gewissen Grad [illegible] klinischen Symptome einer Labyrinthektomie erinnern Die klinischen Symptome einer vestibulären Störung verbunden mit einer sich auf die Crista ampullaris lokalisierten Schädigung werden besprochen

High frequency ultrasound is also used for destroying biological tissue. This effect has been used mainly for treatment of patients with Menière's disease with the intention to selectively reduce or eliminate the vestibular function of the inner ear with preservation of hearing. Up to now more than 200 patients have been treated at the Otolaryngological Clinic, Uppsala, with this method, producing good results (Sjöberg *et al.*, 1963; Sjöberg, 1964; Stahle 1964; Stahle & Sahl, 1964; Sjöberg & Stahle, 1965; Johnson, 1966). The ultrasonic instrument is constructed in Uppsala. Its transducer is fitted with interchangeable tips of metal and teflon.

The apparatus has been tested on pigeons and "Schlieren" optics have been used to study the penetration of ultrasound in varying bone thicknesses.

We employ a new irradiation technique, under which the operation cavity is dry with only a single drop of saline solution under the transducer tip for coupling. By means of a stereo microscope we are able to direct the ultrasonic beam to the exact anatomical location of otoliths and semicircular canal ampullae. It is thus possible to avoid irradiation of the facial nerve and the cochlea.

A drawback is the high absorption of ultrasound in bone. This hinders energy from penetrating the labyrinthine wall and reaching the neuro-epithelium in the inner ear. It has been found necessary to reduce the labyrinth wall thickness by burring to the order of a few tenths of a millimeter. An optimum thickness must be reached in order to reduce the amount of ultrasonic absorption.

In determining the thickness of the otic capsule preparatory to ultrasonic irradiation, we have been guided by observing the non uniform porous structure of the enchondral bone. The "gray or blue line technique" has not found application in our approach, since we aim the ultrasonic beam toward a region just behind the lateral semicircular canal, under which area lie the ampullae and vestibulum. An instrument making possible the measurement of the bone thickness at this point would be of immeasurable value in improving and simplifying our irradiation procedure.

We have been led therefore *to investigate the possibility of employing ultrasonic techniques for the measurement of the bone thickness in the otic capsule*. It would be highly desirable to be able to determine the thickness at a given point to an accuracy of ±0.1 mm at a minimum thickness of about 0.2 mm.

Along with this, our interest has leaned toward a more general study of the thickness of the otic capsule and otosclerotic foci therein. It is our opinion that during an operation for chronic otitis the possibility of charting the cavity's wall and underlying structure by means of an ultrasonic probe could be of great value.

A premise is, of course, that the dead time due to ringing of the transducer as well as a temporary amplifier paralysis caused by the high

STUDIES OF THE OTIC CAPSULE

I. Reduced Dead Time Ultrasonic Probe for Measurement of Bone Thickness

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Experiments have been undertaken to construct a device for measurement of the thickness of the otic capsule in order to improve the ultrasonic irradiation technique in the treatment of Menière's disease. Because of absorption of ultrasonic energy within the bone, it has been found necessary to reduce the thickness of the bony labyrinthine wall to considerably less than 1 mm in order to obtain optimum destructive effect upon the labyrinthine epithelium. Up to now the guiding parameters have been the characteristic structure of the enchondral bone or a translucent canal.

It would be highly desirable to be able to determine the thickness of the bone at a given point down to a few tenths of a millimeter with reasonable accuracy. That this can be done by the application of a new method for reducing the dead time usually associated with ultrasonic echo instruments, appears reasonably certain. A preliminary model operated at approximately 4 Mc. has reduced the conventional dead time corresponding to several centimeters of tissue depth to one or two millimeters equivalent depth.

Applications for an instrument of the present capabilities within the medical field are numerous.

INTRODUCTION

Applications of ultrasonic echo methods in technology and medicine have increased greatly within the last few years. Flaw detection apparatus for metallurgical use head the list for variety and innovation. The special needs of medicine have resulted in numerous instruments aimed principally at this field. Here can be mentioned devices for studying the mid brain echo, eye dimensions, calcifications in the heart valves, the pregnant uterus, mammary tumours and enlargements of the liver. The majority of these devices suffer from a common fault, namely a rather extended dead time following the transmitted pulse due to *ringing of the transducer* and amplifier paralysis. In many instruments this period corresponds to several centimeters of tissue depth.

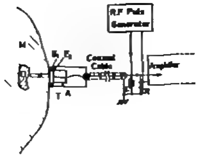

Fig. 1 Loaded transducer and circuitry

thickness of a sintered silver-glass mixture having an impedance possibly quite different from that of either transducer or absorber The transition between, say led zirconate-titanate electrode material and absorber may in practice be the cause of as high a degree of reflection as the impedance mismatch between T and A itself

Eliminating Amplifier Paralysis

The use of a single transducer system as becomes necessary especially when a small region is to be examined, adds to the complexity of the problem in that the generally very high amplitude driving pulse is not only fed to the transducer but simultaneously appears at the input to a high gain amplifier A conventional radio frequency amplifier made up of cascaded tuned stages suffers, as a result, a temporary paralysis which may extend over several microseconds. As was pointed out in the introduction, our aim was the measurement of bone thickness of the order of 0.2 mm, which corresponds to an echo d lay of something less than 0 15 microseconds. Thi condition defines to a large degree the working limits of the ystem as it will eventually take form First of all. it becomes necessary t use a short enough driving pulse that it may be highly damped by the time the desired echo arri es at the amplifier input. This pulse need consist only of one half-cycle of the transducer frequency essentially hock-excit ing the ceramic blank. By choosing a transducer frequency of say 10 0 me sec the time requirement m y be satisfied. The degree of damping applied electrically as well mechanicall will determine the resolution obt in ble

Tw steps may be tak n to minimize amplifier paralysis. The first i to el minat ll l ng-time constant grid circuits. In radio frequency amplifiers thi i most easily ccomplished by placing tuning inductances between grid nd ground or u ing tran f rmer coupling Second, one may make use f the non-l near characteristics of point-contact diodes shunting the circuit. Here high mplitud pulses re presented by low resi tance—chosen to be appreci bly lower than th tage impedance—wherea a very low ampli tud ignal will rem in within the region of curv ture thus being relatively

driving pulse can be reduced to an absolute minimum. Results to date are far from this goal but the evaluation of a new and promising approach has been carried out, the results of which form the basis for this preliminary paper.

THE PROBLEM

Instrument Dead Time

Efforts to reduce the dead time of transducers employed for flaw detectors as well as medical diagnostic instruments have generally been based on a heavy damping of the piezoelectric blanks by means of cast backings of a highly dissipative nature, having acoustic impedances as close to those of the transducer materials as possible (Kossoff *et al.*, 1964). For the most part these employ tungsten or other metal loaded epoxy resins poured over the back electrode of the transducer, filling a volume of several cm³, where they are allowed to polymerize to a solid mass. By proper choice of metal and its careful dispersion throughout the resin, a relatively good impedance match may be obtained with appreciable suppression of spurious responses. Aside from the decrease in dead time, this transducer loading becomes imperative if a high degree of signal resolution is desired.

The problem may be illustrated by Fig. 1. Electrically, the transducer T will be coupled to the remainder of the system via two electrodes E_1 and E_2, most often, in the case of a piezo-ceramic, consisting of fired-on layers of silver mixed with a low melting point glass in powdered form, having a thickness as much as one or two tenths of a millimeter. An electrical pulse fed to the transducer by means of the coaxial cable connecting the probe with the pulse generator indicator unit will generate an ultrasonic disturbance within T, which, in turn, will travel towards E_1 and E_2 in equal proportions. Until such time that contact between transducer and a medium M to be studied is made, energy travelling toward E_1 will be wholly reflected and directed toward E_2. Energy impinging upon E_2 will, if no absorber A is present, simply be reflected back towards E_1 and so forth until internal losses have dissipated the signal.

The addition of an absorber results in a portion of the energy reaching E_2 continuing on into the absorber itself, the remainder being reflected back into T. This ratio between reflected energy and total energy falling on E_2 is expressed by the following power reflection coefficient:

$$R = \left(\frac{Z_A - Z_T}{Z_A + Z_T}\right)^2$$

where Z_A is the effective impedance of the absorber and Z_T is the acoustic impedance of the transducer material. The ideal conditions so easily expressed on paper are not often as easily realized in practice. Electrode E_2 may, in the case of a ceramic transducer, consist of a not insignificant

short lifetime charge carriers or preferably point-contact diodes, which generally exhibit charge carrier storage effects to a lesser degree

The Delay Line Probe

In order to achieve the best possible transducer one would wish to couple the ceramic blank firmly to a material having properties identical to that of the transducer material itself—perhaps an extended bar of the same transducer ceramic. For practical reasons, this bar would have a rather short extension giving rise to echo returning to the transducer within relatively few microseconds after the driving pulse. Since we have been concerned here principally with observing echos from very near lying structures, the presence of strong echos occurring at some later time need be of no concern, as long as the time interval between driving pulse and echos from the end of the bar is sufficiently long to allow observations of all that which is desired. Since also there exist several materials whose acoustic impedances are close to those of the transducer ceramics, one is presented with a number of possible combinations from which to construct a delay line to store unwanted spurious responses during the period under which observation of external echoes is to be made. Fig. 3 illustrates the constructional features of such a delay line probe.

For the case shown in Fig. 3 the delay medium loading the transducer is a metal bar which in itself forms the hot electrode and must be isolated from the ground. Because of the high capacitance of the ceramic transducer stray capacitance between delay bar and the outer shield can easily be made low enough so that its presence is of no consequence.

An advantage of the delay bar serving as transducer electrode is the possibility of eliminating the fired-on electrode thus bonding ceramic directly to the metal. Successful results with a construction of this type are wholly dependent upon producing an as nearly perfect bond as possible between the two material (Spaeth, Rogers & Johnson 1953).

EXPERIMENTAL RESULTS

In order to hold in good contact with the bony walls of the otic capsule within desired area the diameter of the probe at the very tip must be no more than a few millimeter; a diameter equal to that of the standard cavitation transducer tip, i.e. 2.5 mm, would be desirable.

Determination of the thickness and extension of otosclerotic foci by measurements of the stapedial footplate and its surroundings or the round window area would require a probe diameter of the order of about 1 mm. Up to now the most successful unit has been built on a PZT-4 ceramic transducer coupled to a titanium bar. Whereas probes of 2–3 mm diameter have been built they have not as yet been satisfactory. Our research

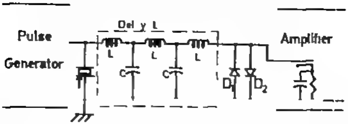

Fig 2 Delay probe transducer followed by a point-diode terminated delay line

unaffected by the presence of the diode Both of these methods have been utilized with good results

Another approach which has been tried with some success, couples the non linear effect of the point-contact diode with a time separation of the transducer—driver combination and amplifier input Briefly this consists of placing an artificial delay line just ahead of the amplifier The delay line parameters are chosen so that when terminated by a suitable diode its characteristic impedance is equal to the forward resistance of the diode near the origin and such that this value is large compared to the diode resistance along its linear region The length of delay required is only that equal to one-quarter-cycle of a sinusoidal driving pulse corresponding to the center frequency of the system It is clear that for very low amplitude signals, such as would be expected from the ultrasonic echos, the delay line is properly terminated The high amplitude driving pulse, when reaching the diode at the amplifier input causes this to conduct heavily in effect short circuiting the delay line Two effects obtain as a result of this first the amplitude of the pulse is reduced at the input grid without loading the driving circuit second the reflection from the shorted transmission line returns to the transducer in phase with its natural period Fig 2 shows the configuration employing a delay line terminated by two opposed diodes

Because of leakage via tube and circuit capacitances, it is of some advantage to apply the diode limiting technique to several of the early stages It is important here to choose diodes which exhibit a minimum of charge storage to prevent the occurrance of an extended pulse "tail" (van der Ziel 1958) resulting from the gradual return to an equilibrium state when slow diodes are pulsed This implies the use of either junction diodes having

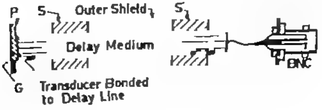

Fig. 3 Basic constructional details of delay line probe

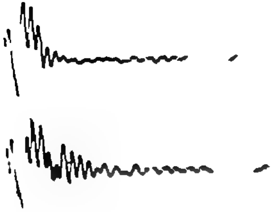

FIG. 6 *a*. Response f d lay line probe only (mplifier A)—upper trace
FIG. 6 *b* Echo from 2 mm thick bone (mplifier A)—l wer trace

and filling the region immediately around the transducer with a polyester potting compound. After this had hardened, external excess was lapped off the transducer urface cleaned and a silver electrode deposited chemically over both transducer and potting compound and on to a portion f the metal shield making a continuous electrical ground. As seen in Fig. 4 tl e outer tube is divided, the second half containing an internal spring contact leading to a BNC coaxial contact at its end

The titanium bar was cut to 10 cm, resulting in an echo delay of some thing over 30 microseconds. Transducer thickness corresponds to a frequency about 4 mc/sec

A thyratron pulse circuit ha been employed for generating the driving pulse Tuning is accompli hed by means of a bank of inductances. The pulse generator and it associated circuitry are shown in Fig 5

A 2D21 thyratron is llowed to operate as a relax tion oscillator its repetition rat determined by the combination RC When the tube fires, the harge ccumul ted by C is lead off the discharge current passing throug the primary of the pulse transf rmer T_p A double-pole-double-throw wit h S select series or shunt placement of a number of induct nces, wi ich m in turn be selected by S for tuning the transducer DI of th del y l n probe A 100 hm, 1 to 120 dB step attenuator i placed ahead f th mplifier to m k possible level mea urements relative to the dri ing pulse Thi method of mea urement liminates amplifier non-line rities, nd y eld the actual relations between pulses of differing ampli tu les, g rdless f uppres i n f higher level signal due to diode limiting, etc the mplifier

The p lse circuit hown generates a driving pulse having a peak-to-peak wi g of ver 100 v lt when terminated by the transducer and the 100 ohm

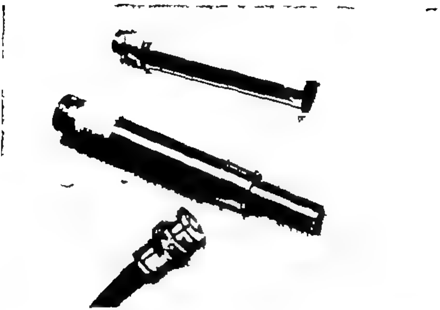

Fig 4 The delay line probe

is just now focussed on this problem However the results obtained with a 10 mm diameter *PZT-4* transducer titanium delay bar combination mounted in a 15 mm O D thin walled shielding tube have been interesting enough to warrant reporting upon

A PZT-4 transducer blank having a diameter of 10 mm was lapped on both sides to remove the original electrodes The titanium bar after turning the ends flat was also finished by lapping Bonding material chosen was a special thin flowing epoxy resin based on an Araldite type MY 740 using a pp methyline dianiline hardener applied very thinly and cured for several hours at 120–130 C

After assembly the delay line was examined for echo and spuriou response level End-of bar echos were found to lie 20 to 26 dB below the driving pulse Undesired signals arising from the transducer and its neigh borhood were found to lie between 1 and 0 3% of the driving pulse amplitude

This bar was now mounted in the shield tube using plastic sleeve spacers

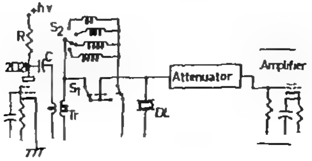

Fig. 5 Thyratron p lse generat r tu f g e ll a l mea l g att t r

FIG. 8 a. Same as 6 a, but amplifier B—upper
FIG. 8 b. Same as 6 b but amplifier B—lower

signals generated in the transducer—however some may be traced to low level signals resulting from reflection effects and ringing of the external circuitry. Total sweep length shown in Figs. 6 and 8 is 10 microseconds, thus the main driving pulse residue extends over approximately 3 microseconds, of which the latter half-portion lies at −40 to −50 dB referred to the main pulse itself external to the amplifier. The echo in Figs. 6 b and 8 b is from a piece of bone taken from the femur ground to a thickness of 2 mm. Because of the somewhat porous structure of the bone attenuation of the ultrasonic signal within the bone is extremely high. The echo level shown here is approximately 40 dB below the driving pulse.

Figs. 7 a and 7 b show a series of echoes obtained from 1.0 mm and 2.0 mm thick high density polyethylene sheets, sweep length 25 microseconds. Here one can see the first echo in the 1.0 mm material overlapping the driving pulse and thereby suppressed, whereas, the same echo for the 2.0 mm case has reached nearly full amplitude. This may be deduced from the only slightly depressed exponential decay curve of the echo train. It is not to be expected that the diode limiting would discriminate against the higher pulses to some extent.

From the above results, it is clear that the method is useable for discerning objects lying as close as 2 mm from the transducer in materials having ultrasonic velocities in the range of 3 mm microsecond and higher. In soft tissues, where the velocity is about one-half of this, the working range can be as close as 1 mm.

Returning briefly to Fig. 1 it is clear that if all energy reaching F could be made to pass into the test material M by reciprocity reflections from a discontinuity D would just as easily pass on to the transducer and be detected. Unfortunately the interface relationships here are such that often, only a fraction of the ultrasonic energy produced within the trans-

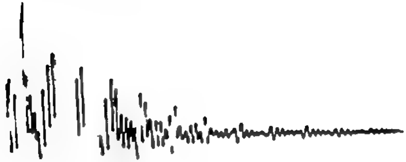

Fig. 7a. Echos from 1 mm thick polyethylene sheet (amplifier A)—upper.
Fig. 7b. Echo from 2 mm thick polyethylene sheet (amplifier A)—lower.

impedance level of the attenuator. Pulse lengths are of the order of 10 to 50 nanoseconds or less.

When an artificial delay line was employed this replaced the tuning inductance in the set up of Fig. 5. Results of this technique were interesting, but called for an artificial delay line of higher quality than the one constructed for the purpose. A length of delay cable shall be substituted in future trials.

A number of modifications were made on the amplifier in order to eliminate paralysis and general broadening of the driving pulse. In fact the amplifier was modified from a stagger tuned wide-band r. f. amplifier to essentially a video amplifier in which circuit parameters were selected to give the required band pass characteristic. Grid-to-ground resistances were made very low leading to the use of coupling capacitances of several microfarads in order to prevent differentiation effects. The tendency towards pulse broadening was also reduced some by decreasing the low frequency gain. This was achieved by reducing cathode and screen bypass capacitances.

The series of photographs in Figs. 6 and 7 were taken with this amplifier (amplifier A). A very short time constant follows the detector so that the rectified signal shows maximum detail. Figs. 8 a and 8 b were taken using a stagger tuned amplifier having limiting diodes across the first three stages (amplifier B).

The residue of the driving pulse seen to the left in Fig. 6 a and 8 a lies approximately 30 dB below the level of the driving pulse at the amplifier input. The disturbances along the base line are due primarily to spurious

One method of achieving this has been to flow a generous amount of thin, uncured epoxy resin onto the surface of the transducer held horizontally in a jig and carefully sprinkling metal powder uniformly over the thin liquid. The metal powder settles down through the resin on to the transducer blank, after which the resin is cured and the top surface planed off. Leaving enough resin that the outermost part is free of metal powder a workable transition layer is obtained. Other similar approaches have been tried as well, all of which have resulted in a marked improvement over the bare transducer. For instance, a construction employing a thin sheet of polyethylene gave an extremely good match to dry skin. That is, it was possible to apply the transducer directly to the skin surface, and without the use of coupling liquids to obtain good transmission of ultrasound through the interface.

CONCLUSIONS

By means of an ultrasonic echo technique it has been possible to measure the thickness of thin tissue layers down to 1 mm.

A new approach to the elimination of dead time associated with pulse-echo diagnostic instruments and flaw detectors, based on the reduction of crystal ringing and amplifier paralysis, has been shown practical. The original aims of our present program of research to measure the thickness of the otic capsule and surrounding structures during operation have not yet met with success, but a working principle has been established which can lead to a solution.

The present design, based mainly on the use of an acoustic delay line coupled to the transducer in order to remove disturbing signals long enough to permit observing desired phenomena, can in its present form be *applied to a number of medical problems*. As examples might be considered examination of subcutaneous regions lying as close as a millimeter or two from the surface down to several centimeters, a region normally not readily examined with standard echo transducers, or perhaps, the determination of degree of atherosclerosis at various points along an artery.

A refinement of the present construction is planned, choosing a higher center frequency, 8 to 10 mc/sec. This we hope will make possible the attainment of the goal of 0.2 mm depth with a resolution of the order of 0.1 mm. Through the use of this method we hope to study closely various parts of the otic capsule under normal and pathological conditions, for example otosclerosis.

ACKNOWLEDGMENT

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TABLE 1

Material	Efficiency of probe $(k')^2$
Saline solution (blood)	0.45
Soft tissue (average)	0.52
Bone (skull)	0.42

ducer can reach the test region M and conversely the reflected signals are only in part detected. If, instead of the power reflection coefficient k discussed earlier, one looks at the expression

$$k' = 1 - \sqrt{k}$$

k' will be a coefficient giving the portion of the impinging signal (in terms of its *amplitude*) which actually passes through the interface. Since we are dealing with amplitude relations, this factor can be more easily related to the height of actual signals observed on the oscilloscope face. Further, we are concerned with a two-way traverse of the signal through the interface, thus the term $(k')^2$ will be a useful way of expressing the relative efficiency of coupling of the present probe to a few common physiological materials—as shown in Table 1 (calculated from Sundén, 1964).

One must remember that the condition defined by $(k')^2$ does not include absorption in the material, partial reflections or scattering, etc., which play a part in reducing the returned echo. We see, however, that, in addition to all other losses, the inefficiency due to impedance mismatch is considerable. Some efforts to improve the situation have been made through the use of coupling elements, placed over the transducer surface to reduce the mismatch. If one chooses a material having an acoustic impedance Z_m equal to the geometric mean of the two materials between which transfer of energy is to be made, where these materials have impedances Z_M and Z_T respectively, that is,

$$Z_m = \sqrt{Z_M Z_T}$$

one can expect complete transfer of energy across the interface. This unfortunately assumes a tuned element—its thickness equal to one-quarter of a wavelength—and, as such, can only with difficulty be applied where broadband circuits are involved.

Experiments with graded impedance transition layers have been performed with some success. The graded impedance layer consists of a thin, built up element bonded to the outer surface of the transducer and made up to provide a gradual variation in impedance from that of the transducer blank to a value equal to or close to that of the material to be investigated.

SINGLE UNIT STUDY OF THE COCHLEAR NUCLEUS IN THE MOUSE

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Single unit study of the cochlear nu leus complex in th mouse was performed. Two types f units were encountered which differed in thei tuni g curves, their threshold xcitability nd their response to increasing sou d stimulation The findings suggest that a type I unit onve) information concerning the frequency of a t ne and the type II unit the int nsity f the stimulating soun L Inhibition with tw t ne interaction was shown to exist in type I units. Attempts were mad to determi e the mode of inhibition in peripheral auditory units. Inhibit ry interbeat tracki g by units i dicates a neural mechanism for the inhibi tion encountered in peripheral auditory units seen du ing two tone inte acti n.

Single units from the eighth nerve and cochlear nucleu in the cat were first isolated by Galambos & Davis (1943) Several studies have appeared since concerning these units and attempts have been made to decode the pattern of unit responses (Kiang *et al.*, 1962, 1965 Moushegian, Rupert & Galambos, 1962 Kat uki Suga & Kanno, 1962)

The present investigation deal with singl unit from the cochlear nucleus in the m use Lorente de N (1933 a b) has described in great detail the cellular architecture f this nucleus in the mouse and made se ral physiological assumptions based on the anatomical findings. In the present tudy an attempt will be made to correlate the neurophysiological results with the histological descriptions of Lorent de N Another interest in thi nimal arises from the fact that several strain of mice carry genes f r heredit ry de fness. The hearing loss is either present congenit lly or appears soon after the animal a quires hearing after birth (Mika lian & Ruben 1964 Mik elian, Alford & Ruben, 1965) It has seemed logical t study the n rmally hearing animal first as a basis on which t correlate and interpret later th findings in these abn rmal mice

METHOD

CBA J mice were u ed Thi train ha been tudied previously in this l borat ry and potenti l were recorded from th round wind w and the

This work w supported by the National I stit tes of Neurological Dise ses nd Blindness, NIH, nd the Alfred P Sloa Foundation

ZUSAMMENFASSUNG

Es wurde der Versuch unternommen eine Methode zur Messung der Dicke der Labyrinthkapsel zu entwickeln Diese Methode soll Ultraschallbestrahlung bei der Behandlung von Menièrescher Krankheit erleichtern

Wegen Absorption von Ultraschallenergie im Knochen ist es nötig die Dicke der knöchernen Labyrinthkapsel auf weniger als 1 mm zu reduzieren Dadurch wird optimale Einwirkung auf das Epithel ermöglicht Die Schichtdicke wurde bisher aus der charakteristischen Struktur des enchondralen Knochens oder aus dem Durchscheinen des Kanals abgeschätzt

Es ist in hohem Grade wünschenswert die Schichtdicke bis hinab zu einigen Bruchteilen eines Millimeters mit entsprechender Messgenauigkeit zu bestimmen Dies kann erreicht werden durch Einsatz einer neuen Methode die es erlaubt die für Ultraschallinstrumente typische Totzeit erheblich zu reduzieren In einer vorläufigen Modellanordnung war es möglich die der Totzeit entsprechende Schichtdicke des Gewebes von einigen Zentimetern auf ein bis zwei Millimeter herabzudrücken

Eine Reihe medizinischer Anwendungen für eine derartig verbesserte Ultraschallmethode lässt sich voraussagen

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FIG. 3. T ning curv for type I nit nd type II it of the cochlea ucleus.

one micron in diameter and their impedance was from 1 to 3 megohms. The microelectrodes were connected to a conventional cathode follower preamplifier system and the responses were observed on a dual beam cathode ray oscilloscope Tektronix model 502. The output of the preamplifier was passed through an audio-amplifier system for auditory monitoring. Pictures were taken from the face of the CRO using a Grass camera. The output from the preamplifier was recorded at the same time on a calibrated two-channel Sony tape recorder type 500 for later studies

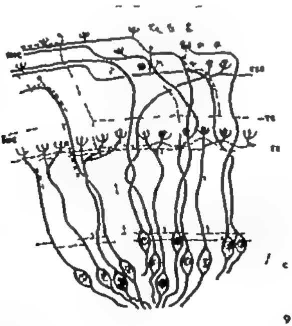


FIG. 4. Schema ic dra ing f cochle r nerv fibe (Smith Rasm sen. By permission) *IHC* Internal hai cell. *EHC* External hai cell. *ESB* External piral bundl *OC* ll o-cochl bundle *SG* Spiral ga glion *TB* T nnel bundle. Solid lines re cochlear nerves. Dashed li es e fferent nerves.

FIG. 1 Electrod track in the cochl n leus (arrow) Mag 40

eighth nerve (Mikaelian Alford & Ruben 1965) The adult mice were anesthetized with intraperitoneal injection of 0 2 cc of a 20% solution of Urethane The head was held in a suitable head holder (Baltimore Inst Co) The surgical procedures employed to expose the eighth nerve and cochlear nucleus have been described in detail previously

The single unit recording was done using glass pipette microelectrodes filled with 3 molar KCl solution The tips of the electrodes were around

FIG 2 Single unit threshold from th cochlea ucl mpared 1 micro lt cochlear potential se lil ity curves in th CBA-J mice

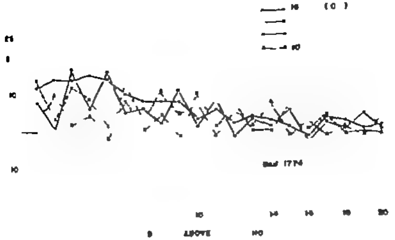


Fig. 7. Rat f chang of pike counts with increasing sound stimulation (one decibel steps in t pe I unit The C.F res als more regular rat f chang tha the other frequencies.

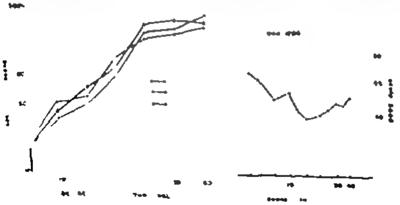
mlera and every other section was stained with hematoxylin and eosin nd mounted for study (Fig. 1)

OBSERVATIONS

The present report i based on bservations of 240 units.

A *Respons Range Threshold and Tuning Curves of Units*

In an earlier study on round window responses in the mouse cochlear potential were obtained f frequencies ranging from 1 kc to above 40 kc. The most sen itive frequencies ra ging between 10 and 20 kc In the study



Response t supvathreshold stimul tion i type II unit Plates les i 1 40 1 an decibel abov threshold.

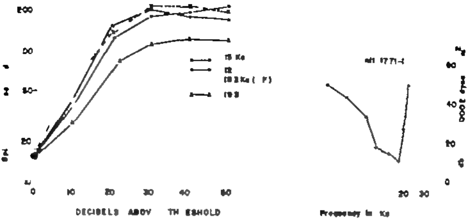


FIG 5 Response to suprathresh ld sound stimulati n in a type I unit 11 teau lev l reached at about 30 decibels bove threshold.

Spike counts of units were made with a Hewlett Packard electronic counter model 521 CR The counter was triggered externally by the same pulse that triggered the tone bursts Spike counts were made for a one second stimulation The pulses were delivered at a rate of one pulse per second

The sound system and calibrating equipment has been reported elsewhere (Mikaelian Alford & Ruben 1965) To demonstrate two tone in hibition identical but separate sound systems were employed To visualize the interference phenomenon of cochlear potentials, a Bruel and Kjaer wave analyzer type 2107 was used and its output was displayed on the face of the CRO

At the end of each experiment the mouse was perfused with physiological saline followed by 10% formalin The head was removed trimmed and decalcified It was embedded in celloidin and serially sectioned at 14

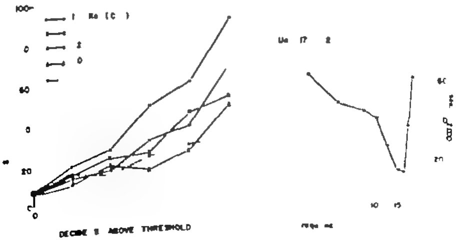


FIG 6 Spik count in ne decibel st ps up t decibel lso-l t lt l l l t pe I unit. The C.F responds with highe spik co t

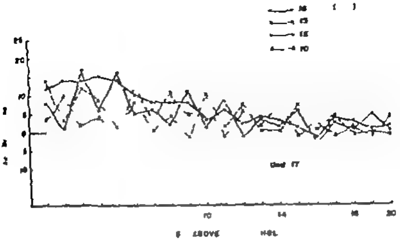


Fig. 7 ... of changes of spike counts with increasing sound stimulation (one decibel steps) ... type I ... The C.F. reveals a more regular rate of change than the other frequencies.

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OBSERVATIONS

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A. *Response Range, Threshold and Tuning Curves of Units*

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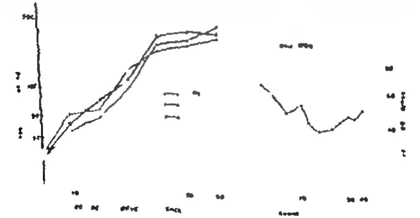

Fig. 8. Response to ... suprathreshold stimulation ... type II ... Plateau ... 10 ... 30 decibels above threshold.

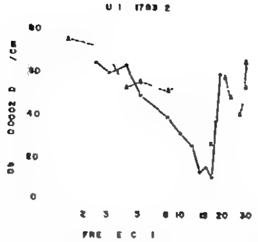

FIG. 9 Inhibitory frequencies plotted for a type I unit The inhibition is produced by both low and high frequency tones.

of single units from the cochlear nucleus the range of responses extended from 400 cps to above 40 kc and here also the threshold responses of units were lowest for the frequencies ranging from 10 to 22 kc (Fig 2)

No special effort was made for a tonotopic localization of frequencies in the cochlear nucleus (Rose, 1960) It was obvious however that units with high characteristic frequencies (C.F) were usually located in the superficial layers of the cochlear nucleus (both dorsal and ventral) and as the electrode was advanced further units with lower C.F s were encountered At this point, it was observed that units encountered in the superficial layers of the cochlear nucleus had lower thresholds than those isolated in its deeper layers On an average this difference in threshold excitability was around 10–15 decibels and was more uniformly present in the dorsal cochlear nucleus than in the ventral Such a finding becomes significant when compared to the histological studies of Lorente de Nó who has subdivided this nucleus into four cell layers (mostly the tuberculum acusticum or dorsal cochlear nucleus) (1933 *a b*) The small cell groups were found in the superficial layers and the larger ones in the deeper layers of the nucleus He showed that the large bipolar cells received much more innervation and made more synapses than the smaller ones He then predicted that these large cells with many synapses would have higher thresholds of excitability than the ones with fewer synapses, because in these large cells many fibers must discharge in order to bring forth threshold excitation The present neurophysiological observations are in agreement with such a physiological assumption

The tuning curves of single units in the mouse were similar to those observed in other animals. In general two types of units were isolated which differed in their tuning curves and their response to increased tonal stimulation Type I units had a sharp cut-off at the high side of the C F with a gradual tapering on the low side and were encountered much more

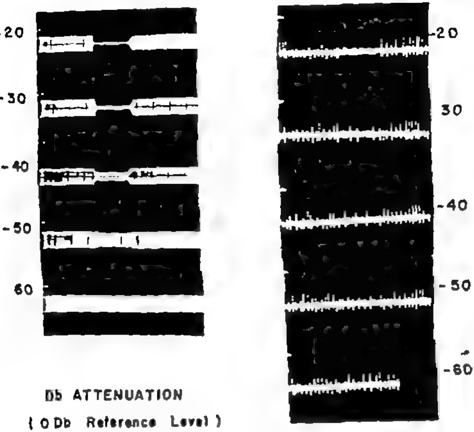

Fig. 10 Left side Cochlea l Interference Cochl potential btained for frequency f 11 kc Interfering tone 18 Kc tone burst Right side I hibitio l the u it R lease of i hibit on nd interference ith gradual decrease in int ity f the i hibiting frequency

frequ ntly The thresh ld of these unit wa u ually very low Type II unit h d gradual tapering on both ides of the C.F and their thresh lds w re h gher (Fig. 3)

B Respon e to Increa ed Sound Intensities

Th re ponse of units to increased inten ities f sound ha been studied pres u ly (Galambos & D v s, 1943 Katsuki, Suga & Kanno, 1962 Ga l mbo & D is, 1944 N m t Sug & Katsuki, 1961) It has been hown th t the rat f discharge in units reaches a pl teau lev l beyond which fu th in rease f th s und inten ity cause either no increase or a d m nutio in pik rat The reducti n of the pikes has been attributed by som to n inhibitory proces in the unit (Galambos & D is, 1944 R se Gal mbos & Hughes, 19 9 Nomoto, Suga & Kat uki, 1964)

In the present studies the response of the unit was studied by increasing the intensity of the sound in 1 decibel steps. The frequencies studied were the C.F. (the frequency with the lowest threshold in the tuning curve) and those frequencies on both sides of it whose thresholds were no higher than 15 decibels from it. Such an arbitrary limitation of frequencies has been based on the pattern of innervation of the organ of Corti (Fig. 4) (Lorente de Nó 1937, Fernandez, 1951, Smith & Rasmussen 1963, Smith, 1961).

In type I units the number of spikes for the different frequencies were similar at the plateau levels (Fig. 5). The frequencies above the C.F. gave usually lower counts independent of sound intensities applied. However, spike counts compared at [illegible] decibel levels above threshold showed clearly that the highest count was achieved by the C.F. (Fig. 6). Similarly the rate of change in spike discharges that occurred with each decibel increase in the sound intensity showed a more regular change of rate for the C.F. than for the other frequencies (Fig. 7).

The findings were different in type II units. Whereas the plateau level in type I unit was attained 20 to 30 decibels above threshold, the type II unit showed only a tendency to do so at 40 to 50 decibels above threshold (higher intensities were not used for fear of damaging the hair cells and for harmonic distortions) (Fig. 8). These observations suggest that units with sharp tuning (type I) convey information about the frequency of a tone rather than its intensity and that type II units seem to convey adequately information about the intensity of the stimulating sound. There has been a trend to relate these two types of units to inner and outer hair cell innervation (Katsuki, Suga & Kanno 1962, Tasaki & Davis, 1955).

C. Inhibition

Inhibition of peripheral auditory units was observed early by Galambos & Davis (1944). The inhibition was observed when a second tone was introduced. Similar phenomena have been subsequently described in other experimental animals including amphybians (Nomoto, Suga & Katsuki 1964, Tasaki & Davis, 1955, Frishkopf & Goldstein 1963). The exact mechanism for this type of inhibition remains obscure. Inhibition by the olivo-cochlear bundle occurs 20 to 40 msec after electrical stimulation of the superior olivary nucleus (Desmedt 1962, Fex 1962); however the inhibition seen by two tone interaction has a short latency period of 2 to 3 msec. Katsuki (1964), using monkeys, came to the conclusion that the inhibition seen during two-tone interaction was probably neural in nature; however, he could not actually determine the inhibiting cycle.

A similar type of inhibition was also seen in the mouse single units. Inhibition could be demonstrated in almost all type I units but rarely was it seen in type II units. Inhibiting frequencies were found to lie usually on both sides of the C.F. (Fig. 9) but sometimes only on the higher or on

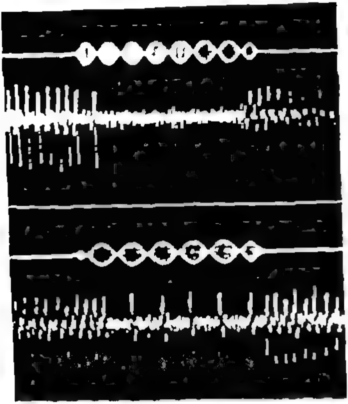

FIG. 11 (See text for planation.)

the l w frequency side The inhibiting frequencies on the high side of the (I did not overlap the response area of the unit, whereas the low fr quency inhibiting t nes usually did It was often observed that a low frequency t ne to which the unit responded produced inhibition in the unit response to a high frequency wh n the tones were presented simultaneou ly Inhibiti n of the low frequencies and pecially in regions bel w 2000 cps were difficult t d monstrat It should be mentioned that un t re p nses in the m use rarely ext nded to frequencies below 2000 cps. Inhib ti n f pontaneous acti ity wa demon trated in those units that ld be dri en lso with sound The phen menon of cochlear interference l n estigated Thi phenomenon has been extensively studied by W ev n & Lawrence (1910 1941 1951) The suppres ion of cochlear potentials esembl ery much the inhibition bserved in ingle unit (Fig. 10) Il n le f thi int rference in unit inhibition i not clear

Th ph n menon f "di -inhibition in i gle unit was in estigated. I t oduct n f a third t ne introduced the f ctor of a difference tone wh h t lated the unit rather than "dis-inhibited" Next, two inhibiting f eque es w e selected with their frequen ies ery close to each other to produce beat tones These wer applied in bursts of 100 msec

long If the frequency of the beats was fast (the fundamentals being in hibitory frequencies) total inhibition was still observed in the unit However when the frequency of the beats was slowed down spikes could be seen tracking the interbeat intervals (Fig 11) Units could track inhibitory intervals up to 60 beats per second while when stimulated units could follow frequencies up to 200 beats per second This difference between the two types of beat tracking may suggest that a unit requires a longer period to recover from inhibition than to recover from its refractory state

DISCUSSION

The behaviour of single units from the cochlear nucleus in the mouse is very similar to those studied in other mammals Frequency tuning in a unit was best demonstrated by the low threshold of the unit at that particular frequency and its response to incr ed tonal stimulation This latter observation was most evident a few bels above threshold and was seen in only type I units At plateau le he type I unit discharged the same number of spikes to the different ncies meaning that the unit s response was not specific at high inten vels For a type II unit less specific response occurs at low threshol but the spike counts keep increasing with increased sound stimul hardly a plateau level occurs This linear response appears to conv quately the informa tion of increased sound intensity

Lorente de Nó (1933) has studied in detail t hlear nuclei in the mouse and proposed several physiological possil One of these has been that large neurons situated in the deeper of the cochlear nuclei make multiple synapses and that these wili higher thresholds of excitability than the smaller cells with fewer ses The present neurophysiological results, comparing threshold exci at various levels in the cochlear nuclei bear out his presumptions (recently similar observations were also reported by Henneman, Somjer rpenter (1965) correlating cell size to excitability in spinal motor neur n their studies and those reported by others, it was shown that the thr f excitability was lower for the smaller spinal motor neurons both t logical and electrical stimulation

Inhibition (lateral inhibition) in peripheral auditory has often been a puzzling question It has been observed in alm ry species studied today and there is yet no clear conception as to its chani m The accumulated evidence points to a neural inhibitory taking place in the cochlea

ZUSAMMENFAS

Es wurden Untersuchungen des Schnec nplexe is mit Mikroelektroden durchgeführt Zwei Arter nt pe gefun den die in ihren Stimmkurven ihrer Schw chen

auf gesteigerten Tonanreiz verschieden waren. Die Ergebnisse zeigen, das ein Typ-I Neuron (unit) Auskunft gibt über die Häufigkeit eines Tones und das Typ-II Neuron (unit) über die Intensität des anreizenden Tones. Hemmung durch Zweitonbeeinflussung wurde in Typ-I Neuronen nachgewiesen. Versuche wurden gemacht um die Art der Hemmung in peripheralen Hörneuronen zu bestimmen. Hemmende „Interbeat tracking" durch Neuronen (unit) deutet auf einen neuralen Mechanismus zur Hemmung hin, die in periphalen Hörneuronen gesehen während Zweitonbeeinflussung, vorkommt.

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